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THE RISK TO THE INFANT IN BREECH DELIVERY

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FOR a decade and a half the problem of fetal and neonatal mortality in breech delivery has been the subject of lively interest and discussion among obstetricians. In 1926 Irving and Goethals (8) reviewed 10 years of experience with this problem at the Boston Lying In Hospital, and the present article is submitted as a detailed survey of the same subject covering twenty-two years in the same institution.

DEFINITION OF TERMS

Since this article is intended to be a clinical study rather than a presentation of vital statistics in a bureaucratic sense, and since it is concerned with all primary breech deliveries over a specified period, stillbirths as well as neonatal deaths are included in the fatalities. A *stillbirth* is defined as a newborn infant which never breathed after delivery; a *neonatal death* is a death which occurred after the establishment of independent respiration. The term *gross mortality* is used to denote the ratio of total stillbirths and neonatal deaths to total deliveries in the series; it is also used to indicate the same ratio among the increments of premature, immature, and mature infants, from which the entire series is derived. *Crude mortality* is used to signify the incidence of stillbirths and neonatal deaths in each group into which the material is divided on any basis other than the maturity of the infant. *Corrected mortality* is the term selected to express the combined stillbirth and neonatal death rate among infants which, theoretically, should have been born alive and should have survived. *Neonatal mortality*, in so far as the term is used in this paper, mostly for purposes of comparison, expresses the ratio of neonatal deaths to living births in any given group or category, and may be computed as *gross*, *crude*, or *corrected*, in accordance with the definitions previously given.

INCIDENCE OF BREECH DELIVERY

From January 1, 1913, to January 1, 1935, 30,655 patients were delivered on the house service of the Boston Lying In Hospital. Of these, 1,219 women were delivered through the pelvis of 1,242 infants by the primary breech mechanism. Those cases of abdominal cesarean section in which the breech presented at the time of operation, regardless of whether the presentation was considered the essential or contributory indication for section, are not included within the scope of this paper. Otherwise all breech deliveries are reported, without regard to the time in gestation when labor occurred; consequently, the series includes infants of all postconceptional ages and all birth weights from the obvious non-viability of miscarriage, through the gradations of prematurity, to full term. The total number of infants born includes those resulting from 23 labors in which each of a pair of twins presented by the breech.

TABLE I.—GROSS MORTALITY IN BREECH DELIVERY, BY YEARS

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %
1913	41	31	5	5	3	0	5	0	2	24.3
1914	22	14	3	5	1	1	2	1	3	36.3
1915	28	18	3	7	1	2	1	2	4	35.7
1916	43	29	6	8	4	2	6	1	1	32.5
1917	52	32	8	12	4	2	9	3	2	38.4
1918	34	22	6	6	2	1	5	2	2	35.2
1919	37	22	7	8	1	1	7	4	2	40.5
1920	29	20	8	1	1	0	1	1	6	31.0
1921	37	28	2	7	0	0	4	1	4	24.3
1922	36	30	3	3	2	1	1	1	1	16.6
1923	41	31	5	5	1	1	1	2	5	24.3
1924	50	37	9	4	2	2	0	4	5	26.0
1925	69	51	8	10	5	1	8	3	1	26.0
1926	79	54	13	12	5	2	8	6	4	31.6
1927	83	68	8	7	2	0	5	2	6	18.0
1928	69	55	10	4	4	1	1	2	6	20.2
1929	55	40	7	8	4	1	5	2	3	27.2
1930	100	78	11	11	1	6	4	6	5	22.0
1931	84	65	12	7	6	2	5	2	4	22.6
1932	86	68	9	9	7	2	5	2	2	20.9
1933	81	63	8	10	2	3	7	1	5	22.2
1934	86	66	12	8	5	4	2	3	6	23.2
	1,242	922	163	157	63	35	92	51	79	25.7

Breech delivery, therefore, occurred in 3.97 per cent of all births during the 22 year period.

GROSS MORTALITY IN BREECH DELIVERY

Of the 1,242 infants delivered, 922 left the hospital alive; 320 were discharged dead, of which 163 were stillborn and 157 died in the neonatal period. The gross mortality, therefore, was 25.7 per cent, or, stated in another manner, there were 131 stillbirths and 126 neonatal deaths per thousand breech births. Figures are available for the years 1924 through 1934, corresponding exactly to the second half of the period covered by this survey, which indicate that in the general incidence of all hospital deliveries 62 stillbirths and 22 neonatal deaths occurred in each thousand births (1). These comparative figures serve to show the marked increase in risk to which the infant is exposed by the circumstance of breech delivery.

CLASSIFICATION OF CAUSES OF STILLBIRTHS AND NEONATAL DEATHS

Table I indicates the gross mortality in breech delivery at the Boston Lying In Hospital during the years covered by this survey. To any student of birth fatalities, it soon becomes evident that cases tend to group themselves into various categories from a clinical standpoint. Thus, certain babies are stillborn following intra-uterine death at some interval before labor occurs, and are therefore delivered in a state of maceration; others are congenitally deformed; some are born prematurely before any hope of "viability" can be expected; certain others succumb to the mechanical hazards of the birth mechanism; and a few are stillborn or die of the effects of accidental complications of birth or of conditions entirely unassociated with delivery. Such a grouping of causes of death can be effected along clinico-anatomical lines with a fair de-

TABLE II.—STILLBIRTHS—CLINICAL DIAGNOSES FROM THE RECORDS

Clinical diagnoses	Total	Macerated	Malformation	Premature	Intercurrent death	Mechanical deaths
Macerated	55	55	0	0	0	0
Non-viable	10	3	0	0	5	2
Maternal toxemia	2	1	0	0	1	0
Maternal infection	1	0	0	0	1	0
Prematurity	3	0	0	0	1	2
Unspecified	18	1	0	0	9	8
Non-viable	8	2	3	0	3	0
Anencephalus	8	0	8	0	0	0
Anencephalus, spina bifida	1	0	1	0	0	0
Hydrocephalus	1	0	1	0	0	0
Hydrocephalus, spina bifida	5	0	5	0	0	0
Congenital ascites	1	0	1	0	0	0
Congenital cystic kidneys	1	0	1	0	0	0
Congenital cyst of mesentery	1	0	1	0	0	0
Generalized dropsy	1	0	1	0	0	0
Multiple congenital anomalies	2	0	2	0	0	0
Asphyxia	36	0	0	0	9	27
Intra-uterine asphyxia	1	0	0	0	1	0
Intracranial hemorrhage	1	0	0	0	0	1
Difficult delivery	1	0	0	0	0	1
Died, difficult delivery (stillborn)	2	0	0	0	1	1
Died, non-viable (stillborn)	4	1	0	0	3	0
	163	63	24	0	34	42

gree of accuracy and tends not only to give a comprehensive view of the fatalities in the series but also to point the way to the computation of corrected mortality. For this reason the 22 diagnoses of stillbirth, listed in Table II, and the 19 diagnoses of neonatal death, computed in Table III, have been condensed into 5 categories or groups, defined as follows:

1. Maceration. This signifies antepartum intrauterine death and decomposition, regardless of causation. Obviously all deaths in this category are stillbirths.

2. Malformation. This signifies gross and tragic anatomical deformities incompatible with life or continuance of life, for which, aside from religious grounds, destructive operations are generally approved. About two-thirds of the deaths in this category were stillbirths, while the remainder occurred in infants born alive.

3. Prematurity. The diagnosis of death from prematurity is, at best, unsatisfactory. Evidence accumulating year by year indicates that many, if not the majority, of infants who die of "prematurity" actually succumb to intracranial or other birth traumas. Therefore in our classification of deaths, we have admitted prematurity as a diagnosis only in the absence of clinical or autopsy evidence of mechanical causation. All dead infants in this category were born alive.

4. Intercurrent deaths. In these cases stillbirth or neonatal death occurred from antepartum infarction, infection, or separation of the placenta; from prolapse of the cord before labor or early in the first stage; from mismanagement of the labor outside the hospital in other hands before admission; from such anomalies, undiagnosable antepartum, as congenital heart lesions; and from incidental diseases which were present in the infant in early neonatal life.

5. Mechanical deaths. In this category stillbirth or neonatal death during or following the act of delivery occurred from asphyxia or trauma, demonstrable either clinically or at postmortem. In this group occur the cases of intra-uterine asphyxia, intracranial hemorrhage, and difficult delivery recorded in the histories, as well as many instances of "prematurity" and unspecified causation. It is in this category that a search for poor obstetric judgment and for mismanagement of labor would find its greatest return.

TABLE III.—NEONATAL DEATHS—CLINICAL DIAGNOSES FROM THE RECORDS

Clinical diagnoses	Total	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths
Atelectasis	3	0	0	0	2	1
Bronchopneumonia	2	0	0	0	2	0
Congenital heart	3	0	0	0	3	0
Congenital heart and bronchopneumonia	1	0	0	0	1	0
Hemorrhagic disease	4	0	0	0	4	0
Anencephalus	2	0	2	0	0	0
Congenital hernia into cord	1	0	1	0	0	0
Congenital distension abdomen (?ascites)	1	0	1	0	0	0
Hydrocephalus	3	0	3	0	0	0
Hydrocephalus, congenital syphilis	1	0	1	0	0	0
Hydrocephalus, spina bifida	2	0	2	0	0	0
Meningocele	1	0	1	0	0	0
Prematurity	93	0	0	86	2	5
Non-viable	8	0	0	6	2	0
Difficult delivery	3	0	0	0	0	3
Transverse section of cervical cord	1	0	0	0	0	1
Intracranial (cerebral) hemorrhage	18	0	0	0	0	18
Unspecified	10	0	0	0	1	9
	157	0	11	92	17	37

Study of the individual records and diagnoses of death, correlated with the classifications of death in Tables II and III indicates a reasonable accuracy of such correlation in most instances. Thus, stillbirths and deaths from asphyxia, intracranial (cerebral) hemorrhage, difficult delivery, etc., fall naturally into the mechanical group for the most part, with a few in the intercurrent classification. The macerated and malformed infants are grouped automatically. The diagnosis of prematurity as a cause of stillbirth is not admitted in the groupings, and "non-viable" stillbirths are found in all cases to be accounted for by reasons other than prematurity. Neonatal deaths from "prematurity" are found to be due to mechanical or intercurrent causation in 7.5 per cent of the cases so diagnosed. The intercurrent deaths prove the hardest of all to classify: while 14 of the 51 were due to unpredictable complications such as maternal toxemia or infection antepartum, and atelectasis, bronchopneumonia, congenital heart, and hemorrhagic diathesis postpartum, the balance, including accidents of labor of one sort or another, might, with some justification, be considered as mechanical; on the other hand, death might well not have occurred but for the fortuitous complication, and the inclusion of such cases in the intercurrent category seems indicated.

Postmortem examination is recorded in 39 of the 320 fatal cases, an incidence of 12.1 per cent. One macerated fetus was thus examined, and three monstrosities. One infant in the premature category came to autopsy, as did 6 who died of intercurrent causes, and 28 of the 79, or 35.4 per cent, who succumbed to mechanical conditions. While in the last named group, confirmatory anatomical evidence of birth trauma or of asphyxia was found in all cases, it must be conceded that the series is disappointing in its lack of postmortem data on infants classed as dying of prematurity.

THE FACTOR OF PREMATURITY AND ITS BEARING ON FETAL AND NEONATAL MORTALITY

Gross mortality among premature infants. It has already been noted that all infants born by the primary breech mechanism are recorded in this series regardless of the stage of gestation in which labor occurred. Some,

TABLE IV.—GROSS MORTALITY IN BREECH DELIVERY, BY BIRTH-WEIGHTS

Pounds	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %
0 —1	3	0	3	0	3	0	0	0	0	100.0
1 —1½	12	0	9	3	4	0	3	4	1	100.0
1½—2	16	0	6	10	1	2	8	4	1	100.0
2 —2½	28	1	13	14	7	3	12	3	2	96.4
2½—3	31	4	8	19	4	1	18	4	0	87.0
3 —3½	40	7	10	23	3	2	19	3	6	82.5
3½—4	37	20	6	11	1	1	9	2	4	45.9
4 —4½	42	23	7	12	4	1	9	3	2	45.2
4½—5	37	24	5	8	2	2	8	1	0	35.1
5 —5½	69	57	6	6	2	2	2	2	4	17.3
5½—6	77	65	6	6	1	3	1	1	6	15.5
6 —6½	135	121	6	8	1	1	0	3	9	10.3
6½—7	117	101	9	7	2	4	0	3	7	13.6
7 —7½	160	144	8	8	1	1	0	2	12	10.0
7½—8	139	130	6	3	1	3	0	1	4	6.4
8 —8½	103	93	2	8	0	1	0	2	7	9.7
8½—9	72	66	4	2	0	1	0	0	5	8.3
9 —9½	44	36	5	3	1	0	0	2	5	18.1
9½—10	18	14	4	0	0	1	0	3	0	22.2
Over 10	24	16	8	0	5	0	0	1	2	33.3
Not recorded	38	0	32	6	20	6	3	7	2	100.0
	1,242	922	163	157	63	35	92	51	79	25.7

therefore, were premature, and it will be well, before discussing the effect of prematurity on mortality, to define the term. Length of gestation as reckoned from the date of the last menstrual period is the usual criterion adopted in determining maturity of the fetus *in utero*, but in any considerable series of cases gleaned from records this standard is frequently untrustworthy. For this reason we have chosen to consider the birth weight of the infant as a more reliable standard, and accordingly classify an infant weighing less than 5 pounds at birth as premature, one weighing over 5 but less than 6 pounds as immature, and one who weighs 6 pounds or over as mature.

It is a matter of general observation that breech presentation is much commoner in pregnancy before the last weeks of gestation than at term. Hence, should labor supervene spontaneously or be induced artificially at any time previous to the tenth lunar month it is reasonable to expect a higher incidence of breech presentation in premature labors than in deliveries at term. Conversely, a given series of breech deliveries should, *a priori*, yield a higher ratio of premature infants than the general ratio of premature to mature infants in the newborn clinic population.

Arranging the infants in our breech series according to birth weights we find, in Tables IV and V, that 246 were premature, 146 immature, 812 mature, and 38 not weighed. The gestational dates in the 38 cases in which weights were not recorded are as follows: 4 to 5 months, 1; 5 to 6 months, 5; 6 to 7 months, 9; 7 to 8 months, 10; 8 to 9 months, 5; at term, 7; information lacking, 1. From these figures one may compute the incidence of prematurity in the series either as 246 cases in 1,204 *weighed* infants, or 20.4 per cent, or, considering as premature all unweighed infants below 8 months, as 271 of 1,242 babies delivered, or 21.7 per cent. Whichever of these figures one prefers, they are both more than three times as high as the 6 per cent (1, 4) incidence of prematurity in the hospital deliveries at large.

TABLE V.—GROSS MORTALITY IN BREECH DELIVERY, AMONG PREMATURE, IMMATURE, AND MATURE INFANTS—INCIDENCE OF PREMATURITY

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %
Premature, by weight	246	79	67	100	29	12	86	24	16	67.8
Premature, unweighed	25	0	21	4	11	4	3	6	1	100.0 70.4
Immature, by weight	146	122	12	12	3	5	3	3	10	16.4
Immature, unweighed	5	0	3	2	3	0	0	1	1	100.0 19.2
Mature, by weight	812	721	52	39	11	12	0	17	51	11.2
Mature, unweighed	7	0	7	0	5	2	0	0	0	100.0 11.9
Maturity unrecorded, unweighed	1	0	1	0	1	0	0	0	0	100.0
Total deliveries, by weight	1,204	922	131	151	43	29	89	44	77	23.3
Total deliveries, unweighed	38	0	32	6	20	6	3	7	2	100.0
Total deliveries	1,242	922	163	157	63	35	92	51	79	25.7

Incidence	By weight, %	Total deliveries, %
Premature infants	20.4	21.7
Immature infants	12.1	12.1
Mature infants	67.4	65.9

The gross mortality in premature infants in this series may be reckoned either as 167 stillbirths and deaths in 246 premature infants delivered, or as 192 fatalities in 271 deliveries. The gross mortality, therefore, is either 67.8 per cent or 70.4 per cent. Eliminating the stillborn, the neonatal death rate amounts to 55.8 per cent or 56.8 per cent, respectively, in the weighed and total groups. These figures are considerably in excess of the 38 per cent neonatal death rate among prematures in the hospital at large for the period 1923 through 1933 (4).

Table IV indicates that among premature breech born infants, stillbirths and neonatal deaths claim more than 50 per cent of those weighing less than 3 pounds, 8 ounces. The neonatal death rate among live born infants is also in excess of 50 per cent below this birth level (Table VI). That the same mortality holds in general for newborn prematures is also shown in Table VI (6). When, however, the weight of the infant exceeds this figure, the risk of birth decreases much more rapidly with increasing poundage in infants in general than in those born by the breech.

The conclusions to be drawn from our figures concerning the incidence of prematurity in breech born babies, and from the gross mortality in this group may be expressed as follows:

1. Prematurity occurs at least three times as frequently in infants born by the breech as in newborn infants in general.
2. Three pounds and 8 ounces is the minimum weight level at which a premature newborn has an even chance of survival, whether born by the breech or any other mechanism.
3. Breech delivery of premature infants is associated with a higher mortality in weight groups above the 3 pound 8 ounce level than is to be found in delivery of premature infants in general in similar weight groups.
4. Not only is prematurity an important factor in the gross mortality of breech born babies: breech birth is an equally important factor in the mortality of premature babies.

Gross mortality among immature infants. In this series 146 babies weighed between 5 and 6 pounds at birth. Twelve were stillborn and 12 died in the neonatal period. The gross mortality was therefore 16.4 per cent of weighed infants, and the neonatal mortality was 8.9 per cent of babies born alive. If we arbitrarily assume that the 5 unweighed infants born between 8 and 9 months were immature, the figures are, respectively, 19.2 per cent and 10.2 per cent. Since general neonatal mortality for immature infants in the years 1932 and 1933 was 3.1 per cent (6), it is evident that breech presentation increases the risk of birth for the immature infant approximately threefold.

Gross mortality among mature or full term infants. The total series of breech born infants includes 812 which, by weight, were classified as mature, together with 7 full term babies whose birth weights were not recorded. Of the weighed babies, 52 were stillborn, and 39 died neonatally; of those not weighed, all were stillbirths. The gross mortality was therefore 11.2 per cent or 11.9 per cent, and the neonatal death rate 5.1 per cent. Since the last named rate in the hospital at large is about 0.7 per cent (6), it would seem that the risk of birth for breech infants is increased at least seven times by the occurrence of such presentation.

Returning to Table IV one sees a strikingly consistent downward curve in gross mortality by weight groups to a minimum at 7½ to 8 pounds, interrupted by a paradoxical irregularity between the 5½ and the 7 pound groups, which may be due to an accidentally low mortality in the 6 pound, or an accidentally high mortality in the 6½ pound group.[1] From the minimum gross mortality of 6.4 per cent among babies weighing from 7½ to 8 pounds, the mortality increases consistently in the groups above this level. Offhand one would suppose that the increasing size of the fetus would account for the increased risk on a mechanical basis, but in the highest weight groups, from 9½ pounds on, the recorded mortality is due more often than not to maceration, malformation, or to intercurrent causes.

A general and comparative tabulation of gross fetal and neonatal mortality in breech born infants. Table VII is inserted at this point to show the gross antenatal, natal, and neonatal death rates in the breech series from 1913 through 1934, parallel with corresponding figures for all hospital deliveries from 1924 through 1934.[1] The strikingly higher incidence of stillbirths and neonatal deaths among breech born infants as contrasted with the occurrence of fatalities among the hospital newborn population at large is evident in both premature deliveries and immature and mature births.

[1]A statistician's delight in a smooth curve might be somewhat dampened by this finding, but he might find solace in a belief that if the 7 unweighed but presumably mature infants happened to fall in the 6 pound group, the mortality of which would then be 14.7 per cent, the regularity of the curve would be restored.

TABLE VI.—GROSS NEONATAL MORTALITY AMONG PREMATURE BREECH BORN INFANTS, CONTRASTED WITH SIMILAR MORTALITY AMONG ALL PREMATURE INFANTS BORN IN THE HOSPITAL

Weight in pounds	1913–1935 Breech series			1923–1934 General series		
	Deliveries	Deaths	Mortality %	Deliveries	Deaths	Mortality %
Less than 1	0	0	0	1	1	100.
1—1½	3	3	100.	9	9	100.
1½–2	10	10	100.	33	32	97.
2 –2½	15	14	93.3	61	55	90.
2½–3	23	19	82.6	84	58	69.
3 –3½	30	23	76.6	112	67	59.8
3½–4	31	11	35.4	143	46	32.2
4 –4½	35	12	34.2	230	45	19.6
4½–5	32	8	25.0	262	29	11.1
	179	100	55.8	935	342	38.

THE EFFECT OF COMPLICATIONS OF PREGNANCY, LABOR, AND DELIVERY UPON MORTALITY AMONG BREECH BORN INFANTS

The figures so far recorded include all breech deliveries through the pelvis over a period of 22 years. It cannot be said that in all cases pregnancy and labor were normal so that the gross mortality among the infants born was due to the mechanics of birth; on the contrary 272 of the infants born were exposed, at some time, *in utero* or *intrapartum*, to one or several complicating factors which in themselves are generally recognized as dangerous to the life of the fetus before or during birth. Though these conditions, as they occurred, are recognized and will be recorded herewith, the number of cases occurring under each heading is in most instances too small to make a thorough analysis of the prematurity factor, etc., worth while. However, it should be pointed out that when such a condition co-exists with breech presentation, the mortality risk should be compared *not only with the risk incurred by an infant breech born of a mother free of such complication but also with the risk incurred by any infant born of a mother in whom such complication is present.* Thus, the breech born infant of an eclamptic mother is subjected to the combined risks of maternal eclampsia and of breech de-

TABLE VII.—GROSS ANTENATAL, NATAL, AND NEONATAL DEATHS IN BREECH DELIVERY, CONTRASTED WITH ALL SUCH DEATHS OCCURRING IN THE HOSPITAL. (EXPRESSED IN THE RATE PER THOUSAND BIRTHS)

		1913 through 1916	1917 through 1920	1921 through 1923	1924 through 1927	1928 through 1931	1932 through 1934
Gross death rate	Hospital series				89	82	73
	Breech series	313	368	218	252	224	221
Miscarriages, premature and non-viable stillbirth rate	Hospital series				36	38	27
	Breech series	74	85	35	67	61	90
Viable infant stillbirth rate	Hospital series				28	28	27
	Breech series	52	98	52	71	64	23
Premature infant neonatal death rate	Hospital series				12	11	9
	Breech series	112	138	61	71	71	75
Immature and full term infant neonatal death rate	Hospital series				14	10	10
	Breech series	74	46	70	42	27	31
Total births	Hospital series				11,750	12,516	10,205
	Breech series	134	152	114	281	308	253

livery; that born of a woman with placenta prævia runs the risk of death from both breech delivery and the effects of antepartum hemorrhage and asphyxia. For these reasons the "complicated" breech deliveries are arranged in Table VIII; the analyses of separate complications are shown, with the mortality in each.

1. Pre-eclamptic toxemia alone was present in the mothers of 105 of the infants delivered. Eleven other babies were born of toxemic patients in whom further complications occurred, such as syphilis, pyelitis, cardiac disease, placenta prævia, ablatio placentæ, and prolapse of the cord.

2. Eclampsia was a complication in 13 of the patients delivered.

TABLE VIII.—CRUDE MORTALITY IN BREECH DELIVERY IN CASES COMPLICATED BY PATHOLOGICAL PREGNANCY OR LABOR, TABULATED ACCORDING TO COMPLICATION RECORDED

Complication	Cases	Well	Deaths	Mortality %
1. Pre-eclamptic toxemia	105	70	35	33.3
Pre-eclamptic toxemia, complicated	11	3	8	72.7
2. Eclampsia	13	4	9	69.6
3. Chronic nephritis	16	4	12	75.0
Chronic nephritis, complicated	1	0	1	100.0
4. Syphilis	11	6	5	45.4
5. Cardiac disease	13	9	4	30.7
Cardiac disease, complicated	3	2	1	33.3
6. Diabetes	3	1	2	66.6
7. Hydramnios	7	0	7	100.0
Hydramnios, complicated	1	0	1	100.0
8. Ablatio placentæ	27	7	20	74.0
Ablatio placentæ, complicated	2	0	2	100.0
9. Placenta prævia	20	4	16	80.0
10. Prolapse of the cord	22	11	11	50.0
11. Miscellaneous	17	10	7	41.1
	272	131	141	51.8

3. Chronic nephritis complicated 16 deliveries; in one other ablatio placentæ was superimposed upon the kidney lesion.

4. Eleven deliveries were in syphilitic patients.

5. In 13 deliveries cardiac disease was a complicating factor. One additional cardiac developed hydramnios.

6. Diabetes mellitus was present in 3 patients.

7. Hydramnios was present in 7 cases, and in one other was associated with placenta prævia.

8. Ablatio placentæ, in addition to the cases herein reported, occurred 27 times. In 2 other patients this condition was complicated by prolapse of the cord.

9. Placenta prævia alone occurred in 20 cases.

10. Prolapse of the cord alone occurred in 22 deliveries.

11. Miscellaneous complications occurred in 17 cases: acute bronchitis, chorea, cystitis, epilepsy, fibroid uterus, hydronephrosis, peritonitis, 1 each; bronchitis associated with cystitis, 1; pyelitis, 5; pyelitis and cholecystitis, 1; pulmonary tuberculosis, 3.

The figures in Table VIII indicate that crude fetal and neonatal mortality in breech delivery occurring in pathological pregnancy or labor is from 33 per cent to 300 per cent higher than the gross mortality in breech delivery in general, and that it is increased to between three- and nine-fold that occurring in uncomplicated delivery (cf. Table XI). Since the various complications are represented by small groups, and since they differ so fundamentally from each other, the tabulation of crude mortality by years and by birth weights yields no significant information

TABLE IX.—CRUDE MORTALITY IN COMPLICATED BREECH DELIVERY, AMONG PREMATURE, IMMATURE, AND MATURE INFANTS—INCIDENCE OF PREMATURITY

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %	
Premature, by weight	106	21	46	39	19	2	33	22	9	80.1	82.2
Premature, unweighed	12	0	11	1	5	2	1	4	0	100.0	
Immature, by weight	42	32	5	5	3	1	0	3	3	23.8	30.4
Immature, unweighed	4	0	2	2	2	0	0	1	1	100.0	
Mature, by weight	106	78	18	10	4	4	0	5	15	26.4	27.7
Mature, unweighed	2	0	2	0	2	0	0	0	0	100.0	
Total deliveries, by weight	254	131	69	54	26	7	33	30	27	48.4	
Total deliveries, unweighed	18	0	15	3	9	2	1	5	1	100.0	
Total deliveries	272	131	84	57	35	9	34	35	28	51.8	

Incidence	By weight, %	Total deliveries, %
Premature infants	41.7	43.3
Immature infants	16.5	16.9
Mature infants	41.7	39.7

other than that shown in Table IX, which summarizes the incidence of premature, immature, and mature deliveries and the crude mortality in each grade. The incidence of 43.3 per cent of premature infants in this group is to be expected, since not only do many of the complications, such as chronic nephritis and syphilis, predispose to premature labor, but others, such as toxemia and placenta prævia, often require termination of pregnancy a considerable time before term. Table X (7) shows that the dangerous complications of placenta prævia, ablatio placentæ, and prolapse of the cord are not only three, five, and five times, respectively, as frequently associated with breech presentation as with pregnancy and labor in general, but are also in each instance productive of a higher mortality among the newborn.

FETAL AND NEONATAL MORTALITY IN SIMPLE OR UNCOMPLICATED BREECH DELIVERY

The preceding paragraphs have demonstrated the tremendously increased risk to the infant in breech delivery in cases in which pathological pregnancy or labor co-exists. Analysis of 970, or 78.1 per cent, of the deliveries in this series, in which pregnancy and labor were free of the dangerous complications herein mentioned, indicates that crude mortality among the newborn was 18.5 per cent, a figure appreciably lower than the gross mortality among all deliveries. This group of uncomplicated deliveries is presented in Table XI, which shows, in marked contrast to the figures from Table IX, that:

1. The crude mortality in the group was 18.5 per cent.
2. The incidence of premature infants was 15.7 per cent.
3. Of the premature infants 62.1 per cent failed to survive.
4. In the immature category 14.2 per cent were stillborn or died.
5. Mature infants showed a crude mortality of 9.5 per cent.

Table XII shows crude mortality among infants in this group by birth weights. The curve obtained is less regular than that shown in Table IV, but is in general similar to it, with the same sharp fall in mortality between the 3 and 3½ pound groups.

TABLE X.—INCIDENCE OF PLACENTA PRÆVIA, ABLATIO PLACENTÆ, AND PROLAPSE OF THE CORD FOUND IN BREECH DELIVERY AND IN GENERAL

Patients delivered with	Breech deliveries: All patients delivered	Incidence %	Mortality %
Placenta prævia	22	1219	1.8	81.8
Ablatio placentæ	31	1219	2.5	74.2
Prolapse of the cord	29	1219	2.3	55.1

Patients delivered with	General consecutive deliveries: All patients delivered	Incidence %	Mortality %
Placenta prævia	228	39,184	0.58	57.9
Ablatio placentæ	128	26,731	0.47	61.5
Prolapse of the cord	335	67,761	0.49	40.0

TABLE XI.—CRUDE MORTALITY IN UNCOMPLICATED BREECH DELIVERY, AMONG PREMATURE, IMMATURE, AND MATURE INFANTS—INCIDENCE OF PREMATURITY

	Deliveries	Well	Still-born	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %	
Premature, by weight	140	58	21	61	10	10	53	2	7	58.5	62.1
Premature, unweighed	13	0	10	3	6	2	2	2	1	100.0	
Immature, by weight	104	90	7	7	0	4	3	0	7	13.4	14.2
Immature, unweighed	1	0	1	0	1	0	0	0	0	100.0	
Mature, by weight	706	643	34	29	7	8	0	12	36	8.9	9.5
Mature, unweighed	5	0	5	0	3	2	0	0	0	100.0	
Maturity unrecorded, unweighed	1	0	1	0	1	0	0	0	0	100.0	
Total deliveries, by weight	950	791	62	97	17	22	56	14	50	16.7	
Total deliveries, unweighed	20	0	17	3	11	4	2	2	1	100.0	
Total deliveries	970	791	79	100	28	26	58	16	51	18.5	

Incidence	By weight, %	Total deliveries, %
Premature infants	14.7	15.7
Immature infants	10.9	10.8
Mature infants	74.3	73.3

Crude mortality in uncomplicated breech delivery will be further discussed later in this article in its relation to corrected mortality in the same group of cases.

CORRECTED FETAL AND NEONATAL MORTALITY IN BREECH DELIVERY

In computing corrected statistics in a review of mortality, the writer is forced to abandon the objectivity of reported figures for a more or less vulnerable position in which opinion must guide him in reaching his conclusions. The present paper is no exception to this rule. From this it follows that the corrected mortality figures of one observer may differ markedly from those of another, due to a difference of premises in making the corrections. For example, King and Gladden, in computing their corrected mortality, exclude cases of babies under 5 pounds, macerated infants, and multiple pregnancies. Caldwell and Studdiford, in their report, omit macerated infants and others under 4 pounds in weight. Taussig deducts macerated fetus, premature infants, twins, and malformations in arriving at his conclusions, but includes one death complicated by prolapsed cord in a case delivered of a pre-eclamptic mother and another complicated by ablatio placentæ. Mohler, in computing a traumatic death rate in breech delivery, excludes infants under 3 pounds, premature and macerated infants, and certain others over 3 pounds in weight. Morton assumes 1,500 grams, or 3 pounds, 5 ounces, as the lower limit of viability in the newborn child, and includes only babies above that level in reporting his series; he calls attention, however, to the difference in prognosis for "viable" infants below and above 2,500 grams, or 5 pounds, 8 ounces. Cannell and Dodek, who include 13 cases delivered by cesarean section in a series of 562 breech infants, exclude premature infants under 5 pounds, 8 ounces, malformations, and macerated fetus, in correcting their gross figures.

This brief summary of methods of correcting gross mortality figures used by various American authors indicates that their respective statistics are not founded upon any common denominator, and hence are not strictly comparable. The present article at least suggests a common denominator, not only by separating the pathological from the uncomplicated pregnancies and labors, but also by separating the premature from the immature and mature infants delivered. Any interested reader who may be so inclined, provided only that he use the English rather than the metric system of birth weights, will find in the accompanying text and tables ample material which he may use to compare with his own figures.

TABLE XII.—CRUDE MORTALITY IN UNCOMPLICATED BREECH DELIVERY, BY BIRTH WEIGHTS

Pounds	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Mortality %
0– 1	0	0	0	0	0	0	0	0	0	0.0
1 –1½	2	0	0	2	0	0	2	0	0	100.0
1½–2	6	0	1	5	0	1	5	0	0	100.0
2 –2½	14	1	5	8	3	3	7	0	0	92.8
2½–3	17	3	2	12	2	1	11	0	0	82.3
3 –3½	22	3	5	14	1	2	11	1	4	86.3
3½–4	24	15	3	6	1	1	5	0	2	37.5
4 –4½	29	18	3	8	2	1	6	1	1	37.9
4½–5	26	18	2	6	1	1	6	0	0	30.7
5 –5½	43	39	2	2	0	1	2	0	1	9.3
5½–6	61	51	5	5	0	3	1	0	6	16.3
6 –6½	115	106	4	5	0	1	0	3	5	7.8
6½–7	95	88	2	5	0	2	0	2	3	7.3
7 –7½	138	126	6	6	1	0	0	2	9	8.6
7½–8	128	119	6	3	1	3	0	1	4	7.0
8 –8½	94	88	1	5	0	1	0	0	5	6.3
8½–9	66	62	2	2	0	1	0	0	3	6.0
9 –9½	37	29	5	3	1	0	0	2	5	21.6
9½–10	12	11	1	0	0	0	0	1	0	8.3
Over 10	21	14	7	0	4	0	0	1	2	33.3
Not recorded	20	0	17	3	11	4	2	2	1	100.0
	970	791	79	100	28	26	58	16	51	18.5

The standard selected for correcting crude mortality in this series is a simple one, e.g., the elimination of all cases in which macerated or grossly malformed infants were born. These categories alone, it seems to the writer, may be safely disregarded, since no amount of obstetrical skill and judgment in the management of labor can prevent either maceration or malformation. The 3 other groups should be included, for the following reasons:

1. Neonatal deaths from "prematurity" must occur in any series in which labor ensues before term. Naturally, as the present series shows, no mature baby dies of "prematurity," but many premature infants do, and a few immatures may. Clifford (5) has called attention to the risk to the premature infant of delivery by various methods, and it may be that the mechanical stress of breech delivery causes more deaths of premature infants than "prematurity" itself.

2. Stillbirths and neonatal deaths from mechanical factors have been shown to occur among premature, immature, and mature newborns. Asphyxia, intracranial injury, and injuries of the cord comprise the bulk of such fatalities, as a result of which obstetrical judgment and the management of delivery are on the defensive when these cases are considered.

3. Stillbirths and deaths of intercurrent causation have been discussed to some extent previously. Some are due to intercurrent disease of the newborn, and hence are unpredictable. Others, though based on the mechanics of labor and delivery, are purely accidental, as illustrated by the case of the multipara who arrives at the hospital with the legs, buttocks, and trunk of the infant born but with the shoulders and head still imprisoned in the birth canal. Corrected statistics should be made accountable for such fatalities though not necessarily *responsible* for them.

TABLE XIII.—CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY, FOR PREMATURE, IMMATURE, AND MATURE INFANTS

	Premature	Immature	Mature	Total
Deliveries	125	100	691	916
Well	58	90	643	791
Stillborn and died	67	10	48	125
Premature	55	3	0	58
Intercurrent deaths	4	0	12	16
Mechanical deaths	8	7	36	51
Mortality per cent	53.6	10.0	6.9	13.6

TABLE XIV.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
1913 –1916(p)	100	73	11	16	4	5	7	2	9	27.	19.7
1916(p)–1919(p)	100	73	11	16	4	2	12	3	6	27.	22.3
1919(p)–1923(p)	100	86	8	6	2	1	4	1	6	14.	11.3
1923(p)–1925(p)	100	82	10	8	3	2	4	4	5	18.	13.6
1925(p)–1927(p)	100	81	8	11	4	1	7	3	4	19.	14.7
1927(p)–1929(p)	100	82	11	7	4	2	5	1	6	18.	12.6
1929(p)–1930(p)	100	84	7	9	1	6	4	1	4	16.	9.6
1930(p)–1932(p)	100	86	7	7	4	2	4	1	3	14.	8.5
1932(p)–1933(p)	100	81	3	16	2	2	10	0	5	19.	15.6
1933(p)–1934	70	63	3	4	0	3	1	0	3	10.	5.9
	970	791	79	100	28	26	58	16	51	18.5	13.6

TABLE XV.—MORTALITY IN UNCOMPLICATED BREECH DELIVERY, IN PRIMIPAROUS AND MULTIPAROUS, SINGLE AND MULTIPLE PREGNANCIES, FOR PREMATURE, IMMATURE, AND MATURE INFANTS.

Primiparous Single Deliveries

	Cases	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
Premature	43	8	12	23	4	6	20	1	4	81.3	78.7
Immature	42	32	5	5	0	1	2	0	7	23.7	20.9
Mature	313	286	15	12	2	5	0	3	17	8.6	6.5
	398	326	32	40	6	12	22	4	28	18.1	14.2

Multiparous Single Deliveries

Premature	55	21	14	20	8	4	17	3	2	61.8	51.1
Immature	33	29	3	1	1	3	0	0	0	12.1	0.
Mature	358	320	22	16	7	5	0	9	17	10.5	7.5
Unrecorded	1	0	1	0	1	0	0	0	0	100.0	0.
	447	370	40	37	17	12	17	12	19	17.2	11.4

Primiparous Multiple Deliveries

Premature	25	16	2	7	1	2	6	0	0	36.0	27.2
Immature	5	5	0	0	0	0	0	0	0	0.	0.
Mature	7	7	0	0	0	0	0	0	0	0.	0.
	37	28	2	7	1	2	6	0	0	24.3	17.6

Multiparous Multiple Deliveries

Premature	30	13	3	14	3	0	12	0	2	56.6	51.8
Immature	25	24	0	1	0	0	1	0	0	4.0	4.0
Mature	33	30	2	1	1	0	0	0	2	9.0	6.2
	88	67	5	16	4	0	13	0	4	23.8	20.2

TABLE XVI.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY

Primiparous Single Pregnancies

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
1913 –1922(p)	100	73	11	16	2	4	10	0	11	27.	22.3
1922(p)–1927(p)	100	81	13	6	3	2	4	3	7	19.	14.7
1927(p)–1931(p)	100	83	7	10	1	4	5	1	6	17.	13.6
1931(p)–1934	98	89	1	8	0	2	3	0	4	9.1	7.3
	398	326	32	40	6	12	22	4	28	18.1	14.2

TABLE XVII.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY

Multiparous Single Pregnancies

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
1913 –1920(p)	100	78	13	9	5	3	2	5	7	22.	15.2
1920(p)–1926(p)	100	88	5	7	1	2	4	3	2	12.	9.2
1926(p)–1930(p)	100	79	12	9	8	1	5	3	4	21.	13.1
1930(p)–1932	100	82	8	10	3	4	5	1	5	18.	11.8
1933 –1934	47	43	2	2	0	2	1	0	1	8.5	4.8
	447	370	40	37	17	12	17	12	19	17.2	11.4

CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY

Table XIII summarizes the corrected statistics in the present series of uncomplicated breech deliveries, and yields a 53.6 per cent mortality among premature infants, 10.0 per cent among immature, and 6.9 per cent among mature babies at term.

Because the tabulated yearly increment of uncomplicated breech deliveries has been irregular, varying from 17 in 1914 to 84 in 1930, the deliveries in this group have been arranged consecutively in Table XIV in blocks of 100 each for the first 900, and the balance in a block of 70. The average crude mortality of 18.5 per cent and the average corrected mortality of 13.6 per cent are thus broken down into blocks, running in general downward from 27 per cent and 22.3 per cent, respectively, in the earlier years to 10 per cent and 5.9 per cent during the last 2 years. Except for a discouraging lapse in 1932 and 1933, the trend of improved results is marked.

Factors of parity and of multiple pregnancy in relation to crude and corrected mortality in uncomplicated breech delivery. Dividing the uncomplicated breech deliveries into groups based on parity and the occurrence of twins[1] the following figures are obtained, as shown in Table XV.

1. Primiparous single pregnancies showed a crude mortality of 18.1 per cent, corrected to 14.2 per cent. The incidence of premature infants was the lowest in the four groups (10.8 per cent), but the crude mortality among prematures was highest, 81.3 per cent.
2. Multiparous single pregnancies yielded a crude mortality of 17.2 per cent, corrected to 11.4 per cent. These resulted in the birth of 12.3 per cent of premature infants, among which the mortality was 61.8 per cent.
3. Primiparous multiple pregnancies yielded a crude mortality at delivery of 24.3 per cent, corrected to 17.6 per cent. This group showed the highest incidence (67.5 per cent) of premature infants; these, however, had the lowest crude mortality (36.0 per cent) among the prematures in the four groups.
4. Multiparous multiple pregnancies showed a crude mortality of 23.8 per cent, corrected to 20.2 per cent.

Table XV, while showing a greater risk to infants born of primiparous mothers than to those born of multiparous, indicates that delivery of mature infants at full term is more hazardous in multiparous than in primiparous labor. Several observers have reported the

[1]Each of two deliveries in multiple pregnancies involved one of a set of triplets.

TABLE XVIII.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY (MATURE INFANTS)

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
1913 –1918(p)	100	86	6	8	1	3	0	3	7	14.	10.4
1918(p)–1923(p)	100	88	8	4	0	1	0	3	8	12.	11.1
1923(p)–1926(p)	100	87	9	4	3	1	0	3	6	13.	9.3
1926(p)–1928(p)	100	89	5	6	1	0	0	2	8	11.	10.1
1928(p)–1930(p)	100	92	7	1	3	4	0	0	1	8.	1.0
1930(p)–1932(p)	100	93	4	3	2	1	0	1	3	7.	4.1
1932(p)–1934	111	108	0	3	0	0	0	0	3	2.7	2.7
	711	643	39	29	10	10	0	12	36	9.5	6.9

TABLE XIX.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY (MATURE INFANTS)

Primiparous Single Pregnancies

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
1913 –1925(p)	100	85	9	6	2	2	0	1	10	15.	11.4
1925(p)–1930(p)	100	93	5	2	0	2	0	1	4	7.	5.1
1930(p)–1934	113	108	1	4	0	1	0	1	3	4.4	3.5
	313	286	15	12	2	5	0	3	17	8.6	6.5

TABLE XX.—CRUDE AND CORRECTED MORTALITY IN UNCOMPLICATED BREECH DELIVERY (MATURE INFANTS)

Multiparous Single Pregnancies

	Deliveries	Well	Stillborn	Died	Macerated	Malformation	Premature	Intercurrent deaths	Mechanical deaths	Crude mortality %	Corrected mortality %
1913 –1921(p)	100	83	10	7	1	2	0	6	8	17.	14.4
1921(p)–1927(p)	100	91	4	5	2	1	0	3	3	9.	6.1
1927(p)–1934	158	146	8	4	4	2	0	0	6	7.5	3.9
	358	320	22	16	7	5	0	9	17	10.5	7.5

same finding and have accounted for it by stating that multiparæ are more apt to give birth to large and overdeveloped infants. Our figures show that multiparous single pregnancies resulted in the birth of 42.4 per cent of mature infants weighing over 8 pounds, whereas of mature infants born of primiparæ only 25.5 per cent occurred in the higher weight groups of 8 pounds and above. Of these, however, the corrected mortality among heavy first born babies proved to be 10.1 per cent, while that among babies born of multiparæ was 7.7 per cent. The factor of overdevelopment in this series, therefore, did not account for the greater mortality in mature infants born by multiparous delivery.

Tables XVI and XVII show primiparous and multiparous single deliveries, respectively, recorded when possible, in blocks of 100, with the crude and corrected mortality in each block. Again, as in Table XIV, the trend of mortality in recent years has been downward.

Crude and corrected mortality in immature and mature infants born by uncomplicated breech delivery. The final groups to be analyzed in this survey are the series of immature and mature infants born near or at term by uncomplicated breech delivery. The latter

are the cases which correspond most closely to those reported by other authors in their statistics of corrected mortality, although some by definition include infants classed in this study as immature. We have seen, in Table XI, that infants weighing between 5 and 6 pounds are subject to a crude mortality of 14.2 per cent; and that 9.5 per cent of mature newborns fail to survive. Table XIII shows a corrected mortality of 10 per cent for immature, and 6.9 per cent for mature, infants.

In Table XVIII the mature infants in this series are arranged, so far as possible, in blocks of 100, to represent the trend of mortality during the 22 years surveyed. Once again the improvement in results of recent years is impressive.

The same block arrangement of deliveries is shown in Tables XIX and XX for primiparous and multiparous single pregnancies.[1]

To summarize, therefore, the mortality figures for immature and mature infants born by uncomplicated breech delivery, we find that:

1. Of 816 such newborns, above 5 pounds in weight at birth, 83 were stillborn or died, a crude mortality rate of 10.1 per cent: excluding the deliveries of macerated and grossly malformed infants, the corrected mortality was 7.3 per cent.

a. Babies weighing more than 5 but less than 6 pounds at birth showed a crude mortality of 14.2 per cent, and a corrected mortality of 10 per cent.

b. Mature infants over 6 pounds at birth yielded a crude mortality of 9.5 per cent, and a corrected stillbirth and death rate of 6.9 per cent.

2. The mortality rates among mature single infants, both crude and corrected, have shown a marked decline during the years surveyed.

SUMMARY AND CONCLUSIONS

1. A review of 1,242 breech deliveries in the Boston Lying In Hospital, beginning with the year 1913 and ending with the year 1934, is presented.

2. The gross combined fetal (stillbirth) and neonatal death rate was 25.7 per cent.

3. It was found that in 272 deliveries, or 21.9 per cent of the total, either the pregnancy was pathological, with such complications as pre-eclamptic toxemia, eclampsia, nephritis, syphilis, diabetes, hydramnios, etc., or labor was complicated by such conditions as placenta prævia, ablatio placentæ, or prolapse of the cord. Since the crude mortality in this group was 51.8 per cent, the effect of pathological pregnancy and labor as an important factor in the high gross mortality is evident.

4. In the 970 deliveries uncomplicated by pathological pregnancy or labor as above defined the crude mortality was 18.5 per cent.

5. Prematurity of the infant was common in both groups and contributed in no small measure to the crude mortality in each. Uncomplicated deliveries produced premature infants in 15.7 per cent of the cases, with a crude mortality rate of 62.1 per cent; pathological pregnancies and labors resulted in the birth of 43.3 per cent of premature infants, with a crude mortality rate of 82.2 per cent.

6. The risk of breech delivery *per se* should be computed only from cases in which uncomplicated labor occurs. Nevertheless it should be borne in mind that this series shows the incidence of placenta prævia, ablatio placentæ, and prolapse of the cord to be respectively three, five, and five times as frequently associated with breech presentation as with all types of delivery.

7. In uncomplicated breech delivery the crude mortality resulting from primiparous single pregnancy was 18.1 per cent; from multiparous single, 17.2 per cent; from primiparous multiple, 24.3 per cent; and from multiparous multiple, 23.8 per cent.

8. In correcting the crude mortality figures in this series, the only cases excluded are those resulting in the birth of macerated infants and grossly malformed babies. Using this standard for uncomplicated breech delivery, we find that the corrected mortality was 13.6 per cent among 916 newborns, subdivided as follows: 53.6 per cent for premature, 10 per cent for immature, and 6.9 per cent for mature infants.

9. The mortality figure of 6.9 per cent, therefore, represents the risk to the living, undeformed, full term infant *in utero* who is destined to be born by pelvic breech delivery in the absence of pathological pregnancy on

[1]The infants born of multiple pregnancies are too small in number to make this type of analysis of value, but the corresponding information may be obtained in Table XV.

the part of the mother, and of hemorrhagic and other accidents of labor due to abnormalities of the placenta or of the umbilical cord.

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ON THE DIFFERENT FORMS OF NON-GENERALIZED FIBROUS OSTEODYSTROPHY

The Localized, the Diffuse Monostotic, the Unilateral and the Monomelic Form

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THE question of localized (non-generalized) osteitis fibrosa is still very enigmatic despite the fact that during the last two decades a great number of investigators have tried to arrive at greater clearness. From the pathologic-histological viewpoint the question is relatively simple in the more common cases, but a conclusive diagnosis is by far not always to be made merely on the basis of the microscopic study of a few slides. The histological picture of osteitis fibrosa is a too frequent response of bone marrow to different damages and stimuli. It may occur in a number of essentially different bony diseases, as inflammatory, neoplastic, metabolic, and simple mechanical disturbances, so that the histological diagnosis of osteitis fibrosa quite often may in the special case be more obscuring than clearing up. It may at least hide as much as it reveals. In a great number of cases it is only a symptomatic but not a nosological diagnosis.

Nevertheless, there is no doubt that a great deal was done by investigation of pathology, and the recognition of localized osteitis fibrosa in all its forms as an essentially benign lesion signifies a great accomplishment. This seems to be especially true for the giant cell tumors or brown tumors which nowadays are considered by the greater number of pathologists as granulomas rather than real neoplasms. According to Lubarsch and many others, they develop following extensive hemorrhage in the bone marrow. The resorption and organization of the hematoma occur with development of non-specific granulation tissue, which may assume tumor-like appearance. Similarly, the cystic forms of osteitis fibrosa have been explained also on the basis of an extensive hemorrhage in the bone marrow, leading to increased pressure within the marrow spaces and impairment of the blood circulation, especially of the venous flow, von Recklinghausen's stage of phlegmasia, again newly introduced by Pommer as an important factor in bone pathology. Bone tissue yields to this augmentation of pressure with osteoclastic resorption, and, by hydropic degeneration of the fibrous bone marrow, bone cysts may develop.

Clinical observations seem to speak in favor of the just mentioned interpretation because of the relatively frequent observation of spontaneous healing of bone cysts and because of the good response to surgery and X-ray treatment. Thus, we quite often find the topic of localized osteitis fibrosa treated in textbooks of surgery with great confidence and optimism as far as treatment and prognosis are concerned. Nevertheless, every surgeon of some experience with cases of localized osteitis fibrosa knows that such cases do not always do as well as one would expect from the textbook descriptions. Local recurrences are quite frequent and functional impairment of the affected extremity is by no means rare. This is especially true for the group of giant cell tumors, which in many respects act quite differently from simple cases of osteitis fibrosa.

For this discrepancy between textbook optimism and greater reservation in practice we thought it worth while to look over the material of localized osteitis fibrosa as it came to observation in the Surgical and Orthopedic Departments of the State University of Iowa.

We do not intend to give here a detailed study of the pathological findings, although a good number of the cases presented have come to histological examination. Neither can it be of greater interest to discuss more extensively the X-ray findings. This has already been done too frequently and a good number of excellent articles are available. Our main task is the classification of the different lesions. It was planned to present the entire material in one paper; for external reasons, however, the giant cell tumors will be reported separately.

[1] Florida Medical Center, Venice, Florida.

November 9, 1933. June 8, 1934. October 8, 1934.

Fig. 1. Case 2. Boy, 8 years old. Cystic lesion in upper metaphysis of humerus, with pathological fracture. Improved by surgical treatment.

We have divided our material of 25 cases into 4 groups.

A. Cystic and solid localized lesions of osteitis fibrosa, 18 cases.

B. Multiple localized lesions, 2 cases.

C. Diffuse monostotic lesions, 2 cases.

D. Osteodystrophia fibrosa unilateralis, 3 cases.

GROUP A. CYSTIC AND SOLID LOCALIZED LESIONS OF OSTEITIS FIBROSA

In group A, the cystic and solid localized lesions of osteitis fibrosa, there were 18 cases, 9 males, 9 females. The ages ranged from 2½ to 42 years; the average being 11.1 years.

	Cases
First decade of life	13
Second decade of life	2
Third decade of life	2
Fourth decade of life	0
Fifth decade of life	1

CASUISTICS ACCORDING TO LOCALIZATION

Upper Metaphysis of the Humerus—4 Cases

CASE 1. Sixteen year old boy who 3 weeks before admission, while playing ball, felt a snap in the right shoulder and could not use his arm after that. X-ray pictures showed a cystic destructive lesion in the upper metaphysis of the humerus and a pathological fracture with good callus formation. No follow-up.

CASE 2. Eight year old boy fell 4 months before admission and complained of some pain in the right arm, which cleared up soon. Three weeks before admission he slipped and fell forward on his arm. There was a sudden moderate pain with disability. X-ray pictures showed a big cystic area on the upper metaphysis of the humerus, the cortex was broken through in one place and reinforced by periosteal bone: signs of a healing pathological fracture. At operation the cyst in the humerus was found filled with brownish gelatinous material of the appearance of an older blood clot. The cyst wall was formed by a layer of granulation tissue, varying in thickness. Careful curetting was carried out, the wound was cauterized with 95 per cent phenol, and vaseline strips and shoulder spica were applied.

One year after operation, there was free motion in the shoulder joint and strength in the right arm was coming back. Patient was clinically improved. X-ray pictures at three different occasions showed that after curetting, the cyst gradually became smaller, the cortex became stronger, but there still remained a very big cavity and it seemed doubtful whether it would ever fill in entirely.

CASE 3. Eleven year old boy had quick bony consolidation after fracture of the right humerus 2½ years before admission. Two years previously he fell and fractured the right humerus. X-ray pictures showed a multilocular cystic lesion in the upper metaphysis of the right humerus with widening of the shaft and thinning of the cortex from within. Patient was submitted to X-ray treatment (five series within 1 year). The roentgenograms taken at different stages of the X-ray treatment show gradual improvement with better calcification; the cystic areas are filling in and the cortex is becoming stronger; the shaft is getting more and more straight.

CASE 4. A boy 7 years old had a fracture of the left humerus 15 months before admission—a slight injury. Fracture was reduced and immobilized for 6 weeks. Healing was good. The day of admission patient fell again on his shoulder and re-fractured the humerus.

Patient brought the roentgenograms taken at time of first injury, which showed a typical picture of a sharply outlined cystic area in the upper metaphysis of the humerus and a recent transverse fracture through the cystic area. Nine months later the cyst had increased to the length of 2½ inches. There was good union of the original fracture and beginning organization of the cyst by bony trabeculation.

At time of admission a fresh subperiosteal fracture could be seen running through the cystic area, with lateral angulation of the fragments. Patient was immobilized in shoulder spica. One year later excellent healing with good correction of the deformity was present. The cystic area had entirely disappeared, and there was only very slight irregularity of the bony structure.

Case of bone cyst in the upper end of the humerus with two pathological fractures. Treatment was by immobilization. The first fracture was followed by increase in size of the cyst, the second by excellent healing.

Upper Metaphysis of the Femur—8 Cases

CASE 5. Twenty-six year old woman. For 4 years dull and aching pain was noted in left hip, as well as muscle spasm. X-ray pictures showed a cyst in the region of the greater trochanter, well outlined and of the size of a 25 cent piece. Hip was im-

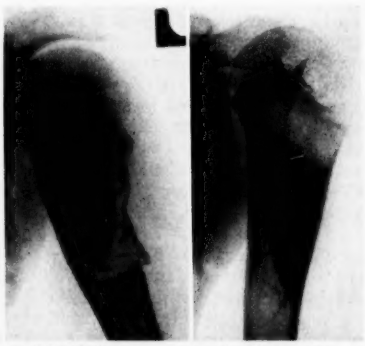
March 19, 1934. July 26, 1934. October 12, 1934. February 1, 1935.

Fig. 2. Case 3. Boy, 11 years old. Cystic lesion of upper metaphysis of humerus, with considerable improvement under X-ray therapy.

mobilized in a plaster cast. Four months later the cyst was filling in; 2 years later the roentgenograms revealed normal conditions, with no cystic area.

CASE 6. An 11 year old boy had limp and pain in the right groin for 9 months. The X-ray picture showed a cyst in the neck and the upper end of the shaft with incomplete fracture. The parents refused to have the child operated upon and a hip spica cast was applied. Seven years later patient was feeling all right. He had no pain, hip motion was limited, and there was some limp. No roentgenological check-up was made.

CASE 7. A 2½ year old girl had limped for 1 month following a fall. The X-ray picture showed a cystic area occupying almost the entire neck of the femur with some periosteal bone production, especially on the outside of the metaphysis. A long hip spica cast was applied. Six months later the cyst had enlarged and the bone was definitely blown up. There was no break in the cortex. One year later (2 years after injury), good healing had taken place with better calcification and a coarse system of new bony trabeculæ.



March 8, 1934. April 17, 1935.

Fig. 3. Case 4. Boy, 7 years old. Pathological fracture through cystic lesion in upper metaphysis of humerus. Good healing under conservative treatment.

CASE 8. A 10 year old girl had a fracture of the upper third of the femur, at which site she had had a fracture before. X-ray pictures showed a big cystic area in the upper end of the diaphysis with pathological fracture and marked varus deformity. There was inward displacement of a piece of the inner cortex. The cortical bone on the outer side was very thin. A double hip spica cast was applied. X-ray pictures, 3 months later, showed good bony healing with filling in of the cavity and a good deal of the deformity corrected. One year later patient started to limp again. Roentgenograms revealed slipped epiphysis.

CASE 9. A woman 28 years of age, 5 months before admission, while doing ordinary housework, began to limp. Motion in hip and knee was quite painful. Immobilization in cast and bed rest were maintained for 5 weeks. X-ray pictures at admission showed a very extensive destructive lesion in the upper end of the femur with extension into the head. There was a pathological fracture through the neck with marked coxa vara deformity. The cortex was thinned, but was not broken through. There was no periosteal bone formation. A hip spica cast was applied. Roentgenograms 1 year later showed good bony union at the site of the fracture. There was better calcification in the cystic area.

September 17, 1927. February, 1928. February, 1929.

Fig. 4. Case 7. Girl, 2½ years old. Cystic lesion in upper metaphysis of femur. Good healing under conservative treatment.

April 13, 1932. October 30, 1932.

Fig. 5. Case 13. Man, 44 years old. Cystic lesion in upper metaphysis of tibia, following trauma. Pathological fracture following curettage.

CASE 10. A 12 year old boy had a fracture of the right femur 3 months before admission to the hospital. Six years previously he had had a fracture at the same site which healed perfectly. Roentgenograms showed a large multilocular cystic lesion in the upper third of the femoral shaft, with marked varus deformity. A subtrochanteric osteotomy was performed to correct the varus deformity. Six months later, good alinement was present with increased density of the cystic area as a sign of healing tendency.

CASE 11. A 5 year old boy had had a limp and slight limitation of motion in the right hip for the last 3 weeks. Roentgenograms showed a big cyst in the upper end of the femur, 1 to 1¼ inches in diameter. At operation, a large cyst of the size of a hen's egg was opened below the greater trochanter, scraped, and cleansed with tincture of iodine and alcohol. A plaster cast was applied. Recovery was uneventful. Patient was seen again 5 years later, when he had no shortening, no limitation of motion—clinically perfect result. No X-ray check-up was made.

CASE 12. A 6 year old boy had had a limp for 1 month. Roentgenograms showed a 2 inch long cystic lesion in the middle and lower part of the neck of the femur. No pathological fracture was noted. At operation, the cyst was opened. The walls were covered by soft granulation tissue which was carefully scraped out. An iodoform drain was inserted, and a cast applied. Roentgenograms, 6 months later, showed good healing, the cavity being almost filled in. No further follow-up has been made.

Upper End of the Tibia—2 Cases

CASE 13. Patient aged 44 years, male, 18 months before admission received a severe blow over the upper end of the tibia from a pick-axe. The skin was broken but the bone was not exposed. The wound healed quickly but quite marked pain in this region persisted. Weight loss was 20 pounds. Roentgenograms showed an extensive destructive lesion, purely osteoclastic, involving the upper end of the tibia with destruction of the anterior cortex. There was practically no periosteal bone production.

At operation, a cavity was found in the upper end of the tibia, filled with rather tough grayish white tissue, which could easily be peeled from the adjacent normal bone. Thorough curetting was done and a plaster cast was applied. Pathological report: osteitis fibrosa.

Following operation, patient was able to walk, but with some difficulty, and pain persisted. He gained 20 pounds. Six months later, he fell and fractured the leg at the site of the cystic lesion. X-ray pictures revealed further extension of the lesion and a fine transverse fracture line. Patient insisted upon amputation, which was performed.

CASE 14. An 8 year old girl had some pain and limp of right leg, following direct trauma to the right tibia 2 months ago. Roentgenograms a short time after the injury showed a small fracture, and 1 month later a cystic lesion in the upper end of the tibia at the site of previous fracture. Roentgenograms at admission showed a slightly lobulated cystic area in the upper metaphysis of the tibia surrounded by some sclerosed bone tissue. Periosteal bone production (callus formation) was also noted.

At operation, the bone cyst was found filled with a yellowish-brown cellular matrix. The area was thoroughly curetted, 95 per cent phenol, alcohol, and vaseline used, and a plaster splint applied. Brodie's abscess, which had to be considered especially from the roentgenological viewpoint, could be ruled out by histological and bacteriological examination.

Lower End of the Tibia—1 Case

CASE 15. A 17 year old boy, 10 years previously had had a severe trauma to the left foot and could not walk for 2 months. During the following 2 years walking was very much impaired, and there were some draining sinuses. Six months ago he twisted his foot, and immediately after he could not walk. The ankle was swollen and painful. Bed rest was maintained for 2 weeks. Roentgenograms showed a clear cystic area of the size of a goose egg, with ex-

April 20, 1933. July 12, 1933. September 1, 1934

Fig. 6. Case 15. Boy, 17 years old. Cystic lesion in lower metaphysis of tibia, treated by curettage and bone chips. Good healing with obliteration of the cyst.

pansion of the bone and thinning of the cortex in the lower metaphysis of the tibia. Practically no periosteal reaction followed. The lower epiphyseal plate was well preserved.

At operation, the periosteum was found to be thickened and edematous. The cortex was very thin, the cyst was filled with serosanguineous fluid and was well outlined with a soft edematous membrane. A thorough curetting was done and bone chips from the tibia were filled in the cavity. A plaster cast was applied. The following month the wound was opened at several places and some of the bone chips became sequestrated. The patient was seen again 18 months after the operation when he had no complaints, the wound was dry, the ankle free, and he had no tenderness. The lower end of the tibia was getting decidedly smaller and the defect was filling in very nicely.

Diaphyseal Lesion—3 Cases

Case 16. A 14 year old girl, 8 years, 5 years, and 1 year previous to admission had had fractures through the diaphysis of the left humerus. The fractures healed well. Roentgenograms showed a typical cystic lesion in the middle of the diaphysis. Four years later the patient stated that the swelling reappeared in the arm with some aching pain. No X-ray check-up was made.

Case 17. A 10 year old girl suffered trauma to the right tibia 6 years prior to admission. She had 2 weeks of bedrest. There was no limp, no pain. Three years later she bumped her leg in the same place and a very painful swelling appeared. Swelling never went down to the original size but seemed to increase after each occasional trauma. On physical examination, a spindle shaped mass at the junction of the middle and upper thirds of the right tibia was seen, with discoloration of the skin, and tenderness. She was unable to walk because of pain.

The periosteum was stripped off and a granulated, soft, yellow tissue was encountered, with numerous cysts. Thorough curetting of cavity (4 to 2½ inches) was done. There were no areas of fracture of the tibia. Long leg cast applied, then a brace.

Roentgenograms 6 months after operation showed at the junction of the upper and middle thirds a multilocular cystic area, involving the anterior cortex, leading to thinning out of the cortical bone, and blowing up of the diaphysis. There was marked anterior bowing of the tibia at the site of cyst, but no breaking through of the cortex. No further follow-up was made.

Case 18. A girl 2½ years of age, had injured the tibia 6 months and 1 month previously. Fracture was of the greenstick variety. Plaster cast was applied. The leg gradually became weaker and swelling increased. Roentgenograms 1 year after the first injury showed marked thickening of the middle of the tibial diaphysis. The diaphysis was interrupted for about 1 inch by a cystic porotic area. Only a thin shelf of bony tissue extended along the outer surface of the cortex as periosteal bone. The soft tissue showed no involvement.

After removal of the eggshell-like cortex the bony cavity was found to be filled in by solid homogenous tissue, which was entirely curetted out. The wound was then treated with 95 per cent alcohol, Dakin's solution, and vaseline strip. Following operation the patient walked with a limp. Four months later the bony swelling began to return and a second operation was performed. A radical curettage with removal of all tissue filling the bony cavity. Ninety-five per cent carbolic acid was applied. Resection of all diseased bone was considered, but it seemed that local removal offered a fairly good chance.

In all 3 cases of diaphysis lesion it appeared certain that the lesion started primarily in the diaphysis and not in the metaphysis. This fact may be emphasized because one finds quite often the statement that diaphyseal cystic lesions are due to gradual displacement of a primary metaphyseal lesion toward the center of the diaphysis. If such a displacement, due to the length growth of the bone by enchondral ossification, were an important

factor, we would expect to find diaphyseal lesions more often.

All the cases presented have been verified by histological examination as far as they came to operation. Cystic and solid forms were considered under the same group of localized osteitis fibrosa and this difference in morphological appearance has been taken only as one of degree. In quite a number of cases, a variable amount of giant cells was present in sections, but we did not think that their irregular distribution and relative scarceness compared with the fibrous tissue which dominated the picture would justify the term "giant cell tumor." It is known, however, that there may be fluent passages from osteitis fibrosa to giant cell tumor as far as the histological picture is concerned.

An important question in cases of localized osteitis fibrosa is the significance of trauma. It is known how difficult it is to rule out definitely traumatic etiology in any skeletal lesion, especially in childhood. For a number of osteitis fibrosa cases, however, trauma seems to have more than accidental importance. At least from the clinical viewpoint, there is no doubt that a great number of cases come to clinical observation following trauma. Quite often, however, the trauma mentioned in the history is insignificant, but it may lead easily to infraction or complete fracture of the diseased area. If roentgenograms are taken at this time, the fracture is evidently pathological; it runs through a cystic area of the skeleton. The bone cysts must have developed insidiously for some length of time previous to the fracture which led to the clinical recognition of the lesion. The pathological fracture has, therefore, no etiological importance for the development of the bone cyst. It is a secondary complication and not a primary causative factor. However, there are quite a number of cases in which definite trauma preceded the occurrence of recognized pathological fracture for some time. In cases of repeated fractures at the same localization especially, in which the roentgenograms at the time of first fracture did not reveal pathological condition of the broken bone, it is quite possible that the first fracture may have led to an extensive hematoma of the bone marrow, the organization of which resulted in cyst formation.

In our series of 18 cases, pathological fracture at time of admission to the hospital was present in 11 (Cases 1, 2, 3, 4, 6, 8, 9, 10, 13, 16, 18). Five out of these had 2 fractures at the same site (Cases 3, 4, 8, 10, 18) and 1 (Case 16) even 3, but in 3 of these cases there is doubt whether the first fracture can be considered as pathological in the absence of definite X-ray findings at that time. The occurrence of the second fracture at the same site suggests, however, a causal connection which most likely is represented by the bone cysts developing after the first fracture. Definite X-ray evidence that the cyst developed 1 month after fracture through the upper metaphysis of the tibia we find in Case 14. Severe trauma, although not leading to fracture, was also present in Cases 13 and 15, and we have reason to believe that in these cases trauma is of primary importance for the formation of a bone cyst.

The 8 cases which did not show definite signs of fracture at the time of admission were complaining of weakness, with limp if the lower extremity was involved. And, as a rule, the symptoms became manifest after a fall. Weakness of the affected bones, pathological fractures, and limp are, therefore, the most important among the early clinical symptoms of localized osteitis fibrosa. Pain, as a rule, is due to the pathological fracture and irritation of periosteum, but not to the disease itself.

The question arises as to the curative importance of the pathological fracture in bone cyst. It is a frequent statement, especially in the German literature, that bone cysts heal after pathological fracture. The explanation given is that the fracture leads to decreased pressure within the cyst. This statement is based partly upon clinical observation, partly, however, upon the assumption that bone cysts derive from bone resorption following increased intermedullary pressure, caused by an extensive hematoma.

In our group there are 7 cases with pathological fracture in which only conservative treatment was followed (Cases 1, 4, 6, 8, 9, 10, 16). One (Case 1) is entirely without follow-up; in 5 instances (Cases 4, 6, 8, 9, 10) definite

February 21, 1929.

Fig. 7. Case 17. Girl, 10 years old. Multiloculated cystic lesion of tibia diaphysis, involving the anterior cortex. Anteroposterior and lateral views.

October 6, 1924.

Fig. 8. Case 18. Girl, 2½ years old. Diaphyseal lesion, involving the cortex. Anteroposterior and lateral views.

improvement could be noticed following the fracture, with increased calcification of the diseased areas in the roentgenograms. Case 4, especially, showed perfect healing of the cyst cavity following the second pathological fracture. One case (Case 16), with two refractures, showed good fracture healing. But 4 years after the last fracture, swelling reappeared and, although roentgenograms were not taken, the patient's description is very suggestive of an increase in size of the bone cyst. So, of 6 cases, apparently only 1 was not improved by the fracture; on the contrary, it showed increase in size of the bone cyst. It is true, however, that the observation time of the 4 cases which showed improvement is relatively short. Only 1 case (Case 6) is followed up for 7 years following first admission; in all the other cases the last control examination was around 1 year after the fracture. Therefore, we can conclude only that the occurrence of pathological fractures in bone cysts may lead to improvement and in some cases even to permanent cure, but we are, on the basis of our material, not able to give any definite statement as to how often a pathological fracture is followed by permanent healing of a bone cyst.

The improvement following fracture can be explained by two factors: the one, already mentioned, is a decreased pressure with its bone resorbing effect; the other is a stimulus to osteogenesis and callus formation, leading to better calcification and the appearance of coarse trabeculation in the roentgenograms.

If this is true and if the pathological fracture in itself has a good influence upon the healing process of bone cysts, then, of course, we have to expect even more from surgical interference.

Of 18 cases 8 were treated surgically, the procedure usually consisting in cutting a window in the thinned cortex and in scraping or curetting out the cavity as thoroughly as possible. Then the cavity is swept out with 95 per cent phenol or iodine tincture and alcohol. In 1 patient (Case 15) bone chips were used from the same bone (tibia) to stimulate bone formation. Two cases have to be ruled out because of lack of control examination following operation. One patient (Case 11) made a good and lasting recovery (5 year observation) following scraping of a cyst in the upper end of the femur. In another case (Case 12), in which the cyst wall was likewise scraped, the

cavity was almost entirely filled by bone tissue 7 months following operation. In Case 2, with 1 year of observation, there are some signs of improvement, but the cavity is still very big and does not show a more marked tendency of getting smaller.

Very definite is the improvement in Case 15, in which, after the scraping of the big cyst in the lower end of the tibia, a good number of bone chips were used to fill the cavity. In this case, 18 months after operation, there was such marked improvement, clinically and roentgenologically, that permanent cure can safely be expected. The sequestration of a number of bone chips a short time after operation did not interfere with the result.

There remain 2 cases (Cases 13 and 18) with decidedly poor results. In Case 13 patient sustained a pathological fracture following curettage of the cystic area in the upper end of the tibia which, 6 months after the operation, did not show any healing tendency. Patient insisted upon amputation. The other case, a diaphyseal cyst of the tibia in a young child of 2½ years, showed progression despite the occurrence of a pathological fracture. The radical curettage was followed by recurrence within 2 months. A second thorough curettage was performed, but the child did not return to the clinic for further check-up.

Of the 6 cases treated surgically, 4 showed improvement (observation time varied from 7 months to 5 years following operation); 1 patient (Case 2), 1 year observation, showed clinical improvement but the roentgenograms still revealed a big cystic area. Two cases (Cases 13, 18) had to be considered failures.

In Case 18, it is true, we do not know how the second operation came out. The first one, however, was very rapidly followed by recurrence. This case, we think, has certainly a tendency to local malignancy. It seems to belong to a certain group of cases in which the bone cyst is filled with solid tissue; it is, therefore, not a real, but a pseudo, cyst. This group can best be termed "borderline cases" to malignancy. They are more frequently observed with giant cell tumors. We shall discuss this group later more in detail.

Somewhat different is Case 13. In this man of 44 years, it is very likely that the severe trauma to the upper end of the tibia resulted in traumatic necrosis of the bone, followed by bone resorption and cyst-like appearance. The thorough curettage weakened the bone even more, and so there is no wonder that a fracture occurred in the weakened weight bearing bone. The leg was amputated despite the fact that there were no definite signs of local recurrence or more marked extension. Decisive was the patient's desire to get back to work as quickly as possible.

The good result obtained in Case 15, in which a large cyst showed very fast and good healing after curettage and grafting of bone chips, the very slow healing in Case 2, and the failure in Case 13 suggest very strongly that the filling of the scraped cavity with transplanted bone is the treatment of choice. Especially in greater cavities and in older individuals in whom the power of osteogenesis has become lowered, it seems that we cannot expect a complete bony obliteration of the cystic defect by spontaneous bone production. This seems, as we shall see, to be even more so in the group of giant cell tumors.

In 1 case (Case 3) instead of surgery, X-ray treatment was followed. Very definite improvement could be seen within 1 year. Although there is a pathological fracture in the history, it seems that the healing process has entirely to be attributed to the irradiation because 4 months elapsed without improvement between fracture and first X-ray treatment. One case is, of course, not enough to draw any conclusions, but it seems that X-ray treatment can be used quite advantageously in a number of cases of bone cysts.

Finally, 2 cases have to be mentioned (Cases 1 and 3) in which healing occurred without any manifest pathological fractures or any special treatment besides immobilization in plaster casts. One case (Case 3) 2 years after admission to the clinic showed good filling in of the bone cysts; the other, 2½ years after admission, does not reveal any pathological structure in the roentgenograms. These 2 cases prove that spontaneous healing of bone cysts is possible with *restitutio ad integrum* of the bony structure, but it is certainly rare. It can, however, not be ruled out that some small fractures which could not be rec-

ognized roentgenologically were present in these cases.

The 18 cases presented were typical inasmuch as they showed a localized lesion of the skeleton in the sense of cystic or solid fibrous osteitis. In quite a number of these cases the X-ray pictures of other portions of the skeleton were taken but did not reveal any pathology. We found, however, in our material 6 cases which do not fit entirely into the group of localized osteitis fibrosa or belong to the generalized form. From a study of the literature, it does not seem possible that a true case of localized osteitis fibrosa ever changes to a generalized form in the sense of von Recklinghausen. There is one case reported by Bergmann, a case of localized osteitis fibrosa, which at the age of 8 years healed well. Thirteen years later, however, the patient developed besides a local recurrence a typical picture of generalized fibrocystic disease.[1] It seems to us, however, that this is only by coincidence and there is no proof that the generalized form developed from the localized one. From the following cases, it will appear that between the monosseous, sharply localized cases and the generalized forms with all the characteristic changes in calcium metabolism we have cases with several similar lesions in the skeleton, each of them well localized; then cases in which one bone of the skeleton is extensively involved, and, finally, cases with a strictly unilateral distribution following certain anatomical structures. However, all of these cases with more extensive involvement of the skeleton do not represent stages of passage to the generalized form. They are typical of the normal blood chemistry and there is nothing to suggest an endocrine disorder.

GROUP B. MULTIPLE LOCALIZED LESIONS

CASE 19. A girl, 12 years of age, had a stabbing pain in the right arm for last 10 months. The roentgenograms showed a multilocular cystic lesion in the lower half of the right humerus with thinning of the cortex and blowing up of the shaft.

At operation, the bony cavities were found filled with solid parts of granulated material and some cystic areas were present. The area was curetted. Two heavy tibial bone grafts were used to fill the defect. X-ray pictures following operation showed a heavy inlay and onlay graft, but the cavity was not filled in entirely. A picture of the tibia from the area from which the bone graft was removed showed good regeneration 2 months following operation. An accidental finding was a small cystic area in the lower metaphysis of the tibia, involving the inner cortex. This cyst was not in relation to the bony defect.

Six months after the first operation, the cystic area of the tibia was exposed. The cyst was well curetted and filled with bone chips. X-ray pictures 15 months after the first operation showed the bone grafts well assimilated to the humerus. The cystic lesion was improved but not healed. There were still some cystic areas present. The cystic lesion in the lower end of the tibia was still present.

X-ray pictures taken at different occasions (from 2 to 5 years after first operation) always showed the same changes. The lesions in the humerus and tibia seemed to be stationary. Pictures of all bones of the skeleton were taken and another small cyst was found in the outer cortex of the left femur at the junction of middle and lower thirds. Clinically, the patient felt fine; only she had occasional pain in the right ankle. The blood chemistry revealed normal values.

CASE 20. A patient 1½ years old, female, had a slight limp of the right leg for the last 4 months. Patient fell the day before admission and hurt her right leg, with marked aggravation of symptoms. Roentgenograms showed to a considerable extent at the junction of middle and lower thirds of the tibia and, a little lower, of the fibula an irregular cystic area with periosteal reaction and reactive bone production around the cystic areas. Similar changes were also present in the upper third of the tibia, especially where the inner posterior cortex was involved. There was anterior and valgus bowing of the tibia.

Patient was given a short leg cast. She returned 4 months later. Laboratory work was essentially negative (tuberculin test, Wassermann reaction, and blood chemistry). Biopsy from tibia showed osteitis fibrosa.

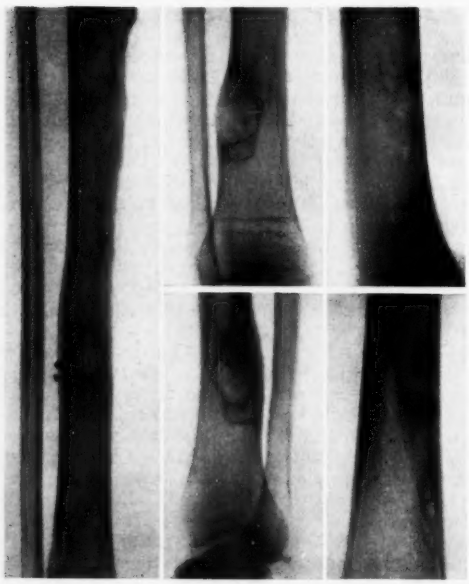
The valgus bowing of the tibia rapidly became worse under the weight bearing stress, despite the brace. The leg was therefore manipulated under anesthesia, and a long leg cast was applied. Roentgenograms 6 months after first admission showed that the lesion had progressed in the lower part of the tibia where a definite cystic area with increased valgus deformity could be seen, following pathological greenstick fracture. At the site of this pathological fracture between middle and lower thirds of tibia a definite pseudarthrosis developed. Considerable periosteal reaction was present, probably due to the fracture (callus formation).

Operation was done 10 months after first admission: Exploration of the site of the deformity revealed pseudarthrosis with fibrocartilaginous tissue interposed between the bony ends; Beck's drilling;

[1] Bergmann, E. Von der lokalisierten zur generalisierten Osteitis fibrosa. Arch. f. klin. Chir., 1926, 141: 673.

April 21, 1927. October 5, 1927. June 17, 1929. August 3, 1932.

Fig. 9. Case 19. Girl, 12 years old. Multiloculated cystic lesion in lower half of humeral diaphysis. Good healing following curettage and bone graft.



e f g

July 28, 1927. August 3, 1932. January 27, 1930.

Fig. 10. Same case, showing circumscribed cystic lesion in the outer cortex of the tibia from which the bone graft has been removed (e). f, Same lesion after curettage. g, Accidental finding of cortical cystic lesion in femur.

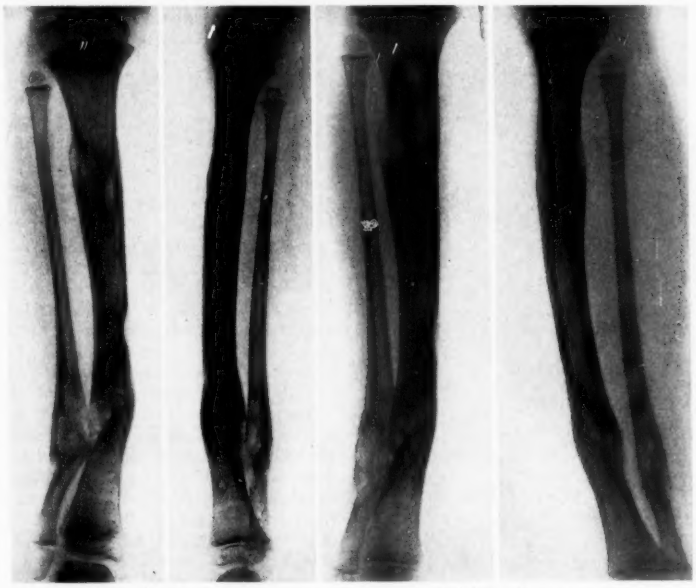
correction of deformity. A cast was applied and later was changed to brace.

Patient was seen at several occasions. She walked with a limp but without pain. She had no complaints except an increase of the valgus deformity of the right leg which is definitely longer than the left. Extensive curettage with massive bone graft from the other tibia was considered.

Some of the roentgenograms in the last case were somewhat suggestive of a connection between the two lesions in the tibia in the sense that there was not a double lesion separated by normal bony tissue but only one extending almost through the entire diaphysis. Without doubt, such an extensive bony involvement was present in the two following cases which, at first impression, seemed to be simple cases of localized osteitis fibrosa. The findings, at time of operation, however, and the slowly but constantly progressive character of the lesion, leading to an extensive invasion of the marrow cavity, pointed toward a separate position among the cases of osteitis fibrosa.

GROUP C. OSTEITIS FIBROSA DIFFUSA MONOSTOTICA

CASE 21. A girl, aged 10 years, complained of an increasing limp during the last year. The limp started following trauma to the right hip when she



November 1, 1933. October 26, 1934.

Fig. 11. Case 20. Girl, 1½ years old. Cystic lesion at junctions of upper and middle, and of middle and lower thirds of tibia, and in lower third of fibula. Pseudarthrosis following fracture.

fell from a sled. Roentgenograms showed a large cystic area in the upper end of the shaft of the femur with irregular, mottled structure in the subtrochanteric region, more purely osteoporotic in the neck. The proximal margin of the lesion was quite sharp; distally it gradually blended into the medullary cavity. The proximal end of the shaft was enlarged, the outer cortex was thinned, and showed a fine break. There was marked varus bending of the femur. Blood chemistry examinations and other laboratory work were negative.

At operation, the cystic area in the trochanteric region was opened and a small amount of serous fluid escaped. The content of the cavity consisted of blood clot, fibrous tissue with calcium deposit. The cavity was curetted and filled in with thin tibial bone grafts. A hip spica cast was applied. Bacteriological findings were negative. Pathology report: osteitis fibrosa.

Six months after the operation the bone grafts were resorbed to a great extent and did not lead to more marked osteogenesis. The lesion in the upper end of the femur had extended downward and occupied almost the entire upper third of the shaft. There was another area of more circumscribed osteoporosis at the junction of middle and lower thirds. Three months later, the roentgenograms were essentially the same, but there was another area of porosis with irregular calcification a little below the first described lesion. The lateral cortex was considerably thinned out. Sixteen months following operation the roentgenograms showed some increased calcification at the site at which the bone grafts were put in. The irregular structure in the femoral diaphysis was now more evident, especially the cortical focus at the junction of middle and lower thirds was quite sharply outlined and defined by some osteosclerosis. All other bones of the body were negative. Six months later (2 years after operation), there was no doubt about the very extensive involvement of the femoral diaphysis and especially of the outer cortex, which was very thin by erosion from within (eccentric atrophy). The process extended from the upper metaphysis downward to the junction of middle and lower thirds. It led to marked osteoporosis and irregular bony structure but without definite cyst formation. Varus deformity of shaft and neck.

Patient had been well all the time; she walked with the typical gait of a coxa vara. At times, after walking a long way, she had some pain at the upper end of the femur. Inasmuch as the X-ray pictures showed a very slow but definite progress of the lesion and deformity, another attempt at curettage, bone grafting, and corrective osteotomy seemed to be indicated.

Second operation (2 years after the first). Through a longitudinal lateral incision, the upper half of the right femur was exposed from the trochanter down-

August 16, 1934. January 2, 1935.

Fig. 12. Case 21. Girl, 10 years old. Extensive cystic lesion in upper end of femur, treated by curettage, bone grafts, and, finally, oblique osteotomy through the diaphysis of the femur to correct the varus bending.

ward. The periosteum was stripped, the cortical bone was found atrophic but smooth. There was considerable thickening of the periosteum over the trochanter. There was also a small defect in the bone, filled by scar tissue, at the site where a window was cut in the bone at time of first operation. The whole upper end of the femur and the medullary cavity were filled with a firm, white tissue of rather high consistency in which a few spicules of bony tissue were included. Only in the region of the greater trochanter some grayish white and soft granulation tissue was encountered. The tissue was expanding toward the cortical bone which showed roughness by erosion on its inner side. At time of operation it seemed that the entire pathological tissue was removed from the upper half of the diaphysis. Normal bony marrow was encountered at the distal end of the saucerization. To judge from the roentgenograms, however, some foci in the lower half of the diaphysis remained. It did not seem wise to correct the deformity of the femur by an osteotomy at the same time. The bone was quite porotic and even more weakened by the radical operative procedure. A hip spica cast was applied.

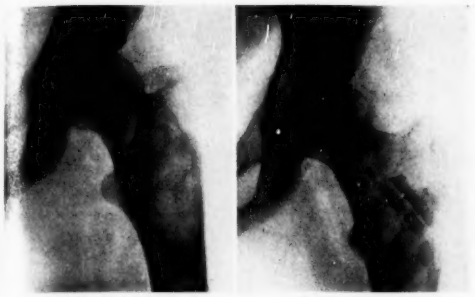
Pathological examination of the removed tissue showed very dense fibrous tissue with relatively few vessels. Bony trabeculæ were imbedded in an irregular way. Most of them were of fibrous type with good calcification of the central portion, whereas the superficial layers were still osteoid. Wherever bony trabeculæ appeared, the bone marrow in their neighborhood was loose, rich in cells and vessels, and stood out very distinctly by its paler stain from the surrounding dense fibrous marrow. It was frequently found that smaller foci of younger and therefore looser bone marrow were almost completely surrounded by a group of bony trabeculæ. In these places the outer side of the bony trabeculæ was rather smooth and the dense fibrous bone marrow showed concentric condensation of its fibers parallel to the bony trabeculæ. The inner surface which faced the loose bone marrow was more irregular, sometimes showing osteoblastic bone apposition, sometimes osteoclastic bone resorption. The cortical bone had undergone marked resorptive changes from the endosteal surface. Fibrous bone marrow was invading the cortical bone along the haversian canals. There was very little periosteal reaction on the outside. The picture was that of a more advanced stage of osteitis fibrosa with extensive scarring of the fibrous bone marrow. In some places the scar formation reached such a degree that large areas were seen without any bony tissue and with beginning hyaline degeneration of collagenous fibers.

Patient made an uneventful recovery. Three months later, to correct the marked varus deformity of the neck and shaft, a long oblique osteotomy was performed. A defect in the cortex still remained. The medullary cavity was found to be filled with the same dense material as at the time of first operation: recurrence of osteitis fibrosa. The bone was curetted out thoroughly. The distal fragment of the femur was brought into abduction to correct the varus deformity. A cortical bone graft was removed from the same tibia and placed in the cavity in the trochanteric region. A double hip spica cast was applied.

X-ray pictures showed very good correction of the deformity following oblique osteotomy. The cast was removed 3 months after operation. The osteotomy was solidly healed and weight bearing was allowed in a short hip spica cast, and 8 months after operation without any support. There was no pain, but there was still a marked limp due to the abductor insufficiency (coxa vara). X-ray pictures 10 months following osteotomy showed perfect healing of the osteotomy with very good callus formation. The upper two-thirds of the femur showed a great number of small cystic areas with a coarse system of trabeculæ between them and very good calcification. Still, from the X-ray pictures, the process seemed to be active.

Before entering the discussion of this unusual and interesting case of osteitis fibrosa, we shall report another case which in many respects, is similar to Case 21.

Case 22. A male, 21 years of age, when 12 years old had a sudden sharp pain in the middle of the shaft of the left femur with muscle spasm. Such an attack of pain recurred frequently, especially when walking to school (2 miles). Three weeks after the initial episode he slipped and fractured the left femur. He was put in traction and cast. At the age of 16 the same type of aching recurred. X-ray pictures were taken and showed cavities in the bone, and the doctor told him that the fracture had been patho-



May 6, 1927. June 6, 1927.

Fig. 13. Case 22. Man, 21 years old. Diffuse lesion of the diaphysis of the femur. Healed pathological fracture in the middle of the diaphysis. Treated by curettage and heavy cortical bone grafts.

logical. He used crutches for 7 weeks. Then, the left leg was as useful again as the right. Same symptoms recurred at age of 20 years. Under symptomatic treatment he improved and at time of admission the only difficulty consisted in an aching pain in the left thigh when he walked longer distances.

On physical examination, a slight fusiform swelling of the left thigh at the junction of the middle third was found, corresponding to the site of the old fracture. Blood chemistry was normal (calcium 11.6; phosphorus 3.8).

X-ray pictures showed a cystic area in the upper end of the shaft of the left femur, extending into the neck of the femur and farther down in the diaphysis. The lower end of the lesion, however, was not included in the picture. The cavity was not sharply outlined.

At operation, the cortex of the upper end of the femur was unusually thin. Under the cortex, very dense, white fibrous tissue was encountered. There was no real cyst formation. The fibrous tissue extended proximally into the neck of the femur; distally it extended beyond the level at which exposure was made. There, however, the cortex did not seem to be involved. Only the medullary cavity was filled with fibrous tissue. This tissue was cleaned out thoroughly with a curette, but no attempt was made to follow the process up into the neck, and distally the operative procedure stopped at the point at which the fibrous tissue narrowed down into the medullary cavity. A heavy, tibial cortical bone graft was cut in several pieces and jammed firmly into the cavity of the femur. Immobilization in plaster splint. Patient made a good recovery.

X-ray pictures 1 month after operation showed the window in the lateral cortex of the subtrochanteric region. The cavity had been filled with a number of heavy cortical bone grafts. The femoral diaphysis showed widening of the shaft with several cystic areas, quite of the same appearance as in the upper third. Most marked widening, spindle shaped

July 30, 1927. February 11, 1930.

Fig. 13.

in character, was present in the middle of the diaphysis where the bone was blown up and the cortex thinned down to a paper-like shell on one side, whereas the other showed definite periosteal bone apposition. Through this area ran an irregular transverse line suggestive of the old fracture which had healed with good bony callus formation. The bony structure was very irregular, mainly consisting of osteoporosis with cloudiness and thinning of the cortex from within (eccentric bony atrophy). The pathological changes extended almost continuously from the upper third down to the junction of the middle and lower thirds. There was no soft tissue involvement.

Patient returned 2 years after the operation, stating that after leaving the hospital he gradually began to use the left lower extremity. Five months ago, however, the original symptoms reappeared in the same intensity, so that he had to use crutches again. Blood chemistry at eleven different occasions showed normal values. On the basis of the X-ray pictures, however, the remote possibility of being a case of hyperparathyroidism was considered. X-ray pictures of all the bones of the body were taken, but were negative with the exception of the left femur. An exploratory operation of the parathyroid glands was performed. All four glands were exposed, but there was no evidence of enlargement in any. None of the glands was removed.

Patient was seen last 3½ years after operation. He had been walking off and on with crutches. He

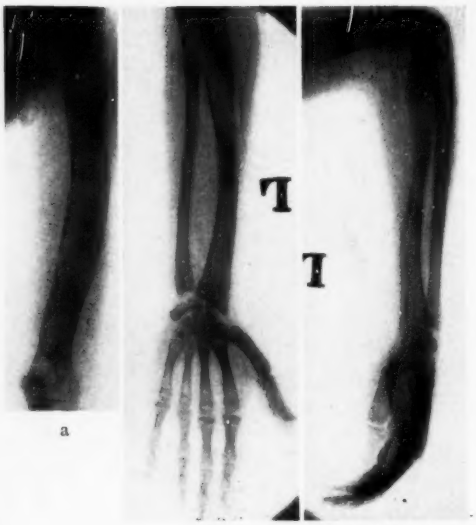


Fig. 14. Case 23.

Fig. 14. Case 23. Girl, 13 years old. Unilateral lesion of fibrous osteodystrophy. Anteroposterior view of the left humerus. Anteroposterior and lateral views of forearm, showing the involvement of the radius and bones of the thumb. Anteroposterior view of left femur with marked coxa vara.

had no complaints. At follow-up examination the X-ray pictures showed essentially the same condition. The bone grafts had taken well and it seemed that the upper portion of the porotic area was filling in nicely, but the porotic changes in the diaphysis were still the same.

Both cases (Cases 21 and 22) have in common the fact that an apparently simple case of osteitis fibrosa—as far as one can judge from the X-ray pictures taken at onset of clinical symptoms—does not show a tendency to heal but rather a slow, but definite, progression, with gradual involvement of the upper two-thirds of the femoral diaphysis. The process remains, however, confined to one bone, and there is no soft tissue involvement. It is a question whether the lesion extends simply through continuity or whether there are several foci, separated from each other by normal bony tissue and bone marrow. The roentgenograms in Case 21 would suggest the latter possibility and so would also the findings at the time of operation, when the lower end of the lesion was reached in the marrow cavity without touching the definite X-ray focus in the lower third. From the study of the histological sections one has to admit, however, that the spreading of the lesion may follow the vessel canals of the haversian systems in the cortical bone, besides the bone marrow spaces, and so roentgenologically apparently isolated medullary foci may still be coherent with the main focus.

Both cases show practically no real cyst formation. The bony cystic areas are filled with dense, white fibrous tissue of relatively high consistency. The density of the fibrous tissue seems to be a characteristic sign of these lesions. It cannot be considered as a simple form of scarring due to the long duration of the process, because the same material had reformed in Case 21 during the 4 months which elapsed between the second and third operations. It is questionable, however, whether the described histological changes with the peculiar interposition of loose fibrous bone marrow in dense almost scar-like fibrous tissue warrants a separation of these cases from other cases of osteitis fibrosa, also from the histological viewpoint. Further pathological study is necessary here to decide this question.

With the tendency to expansion goes also a certain resistance to surgical procedures. Case 21 was operated upon three times and still showed roentgenographic signs of activity. The same is true with Case 22, in which the

January 19, 1935.

Fig. 15. Case 24. Female, 23 years old. Diffuse cystic involvement of the diaphysis of humerus, radius, and bones of the thumb.

fibrocystic process could not be stopped by an extensive curettage and bone graft operation. It is true that, despite the most thorough removal of the pathological tissue, in none of the cases of osteitis fibrosa can one be sure that all tissue has been removed. However, this does not seem to be necessary, as many cases responded well to the routine surgical treatment. Osteitis fibrosa is not a neoplastic, but a dystrophic, disease of the bony tissue, and the cleaning out of the "diseased" tissue aims more at stimulation and making room for new and normal bone growth than at radicality in the sense of surgical attack of a tumor. But this is what, for some unknown reason, this type of case of osteitis fibrosa lacks: the endosteal bone production in a very extensive portion of the diaphysis does not lead to normal bone but to dense fibrous tissue with a few

Fig. 16. Same case, showing the involvement of the first metacarpal bone and first phalanx.

bony trabeculæ of primitive fibrous bone tissue. The periosteal bone formation in these cases is apparently normal; as long as the cortical bone is still present, the periosteal surface is smooth and nothing suggests a more marked participation of the periosteum in the pathological process; the latter seems to be confined entirely to the bone marrow. However, if there is a pathological fracture or if following operation a larger defect in the cortex has to be filled in, a more adequate stimulus is exercised upon the periosteum, which then reveals its normal power to osteogenesis. This factor could be very well observed in both the cases.

From the study of these 2 cases and from observation of Cases 13, 16, 18, and 20, it appears that there are certain cases of osteitis fibrosa (of the solid, not cyst-forming type) which show definite signs of progression and recurrence despite surgical interference. They cannot be called osteitis fibrosa localisata because there is no real localization strictly speaking; it is better to speak simply of a monosseous type of osteitis fibrosa. Such cases make the usually good prognosis in cases of osteitis fibrosa somewhat doubtful.

a a b

Fig. 17. Case 25.

If we neglect Cases 19 and 20, in which more than one bone was involved, we may state that all the other cases, even if as extensive as Cases 21 and 22, were monosseous lesions with essentially normal blood chemistry. There was nothing to suggest a metabolic disorder on the basis of which the bony lesion could have developed. We must assume local irritative factors in the bone marrow which lead to the characteristic picture of osteitis fibrosa. The presence of more than one circumscribed lesion in different parts of the skeleton, however, makes it not unlikely that at least for a number of cases a certain predisposition of the skeleton to fibrocystic osteodystrophy has to be assumed, probably upon an embryological basis.

This is even more so if we find cases in which the distribution of osteitis fibrosa follows certain anatomical structures which make it certain that the lesion must be caused by intrinsic (endogenous) and not extrinsic factors; as for instance, trauma. We had the

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Fig. 17. Case 25. Female, 22 years old. Diffuse involvement of the left femur, less marked of left tibia. Strictly unilateral.

opportunity to study 3 cases (Cases 23, 24, and 25) with strictly unilateral distribution of the dystrophic lesion. One case had been previously reported by one of the authors (E. Freund) and the term osteodystrophia fibrosa unilateralis was suggested for this type of lesion. We report here briefly the case again.

Case 23. A 13 year old girl, at age of 5, began to limp. When 6 years old she fractured the left femur. There was solid bony union after 1 year of traction and fixation in a plaster cast. Her mother stated that the left leg had been bowing progressively during the last years. On physical examination one found a well developed white girl with marked asymmetry of the face and extremities. Especially the left lower extremity showed a marked anterior and varus bowing. X-ray pictures of the skull, spine, pelvis, and bones of the right extremities did not reveal pathological changes. The left humerus revealed definite hyperostotic porotic changes involving almost the entire diaphysis. Only in the distal end and in the upper epiphysis could normal bone structure be seen. There was an almost uniform and equal thickening of the diaphysis. The cortical bone was markedly thinned out and formed only a very thin bony layer which, however, in no place was completely interrupted. The surface of the diaphysis was smooth, and there were no signs of active periosteal bone apposition. The shadow of the bone was cloudy and porotic; only in a few places could a definite structure be seen. These areas probably represented areas of spongy bone where the pathological changes had not yet appeared. The picture was that of diffuse osteoporosis without cyst formation. In addition to the marked increase in thickness, the diaphysis showed also a distinct increase in length (three-fourths inch), despite some bowing in the middle third. There were no signs of recent or healed fractures.

Lesions similar to those of the humerus were seen in the diaphysis of the left radius and in the bones of

the thumb. Essentially the same structural changes were also present in the left femur, only the epiphysis of head and greater trochanter, the distal metaphysis and condyles were spared. Of both bones of the left leg, only the tibia was involved. Almost the entire diaphysis showed the same hyperostotic porotic process which led to an increase of thickness and length, resulting in bowing of the tibia. There was marked valgus deformity at the junction of middle and upper thirds. The changes in the left foot corresponded to those in the left hand; the bones of the big toe only were involved. There was also some irregularity in the bony structure of the first cuneiform bone and possibly of the scaphoid. But it was difficult to ascertain whether these changes were due only to atrophy resulting from disuse.

For further information, a biopsy was performed at the junction of middle and lower thirds of the left tibia. The histological picture was that of osteitis fibrosa. Blood chemistry showed normal values (calcium 11.1 milligrams and phosphorus 3.9 milligrams); phosphatase were increased to 32.5.

Because of the roentgenological and histological findings von Recklinghausen's osteitis fibrosa was considered as a diagnosis and the parathyroid glands were explored. No parathyroid adenoma was found. The two lower parathyroid glands were removed. The histological findings were normal.

A corrective oblique osteotomy was performed with the electric saw, in the same manner as in Case 20. There was not good bony callus formation before 6 months. The patient showed good correction of the deformity and was walking in a hip spica brace. Frequent roentgenological control examinations did not show appreciable changes since first admission.

Case 24. A woman, 23 years of age, when 8 years old fell 4 feet and broke the right humerus in two places. This healed with deformity in normal time. At the age of 10 she was thrown from a horse and fractured her right wrist and the lower end of the right humerus. This healed in 4 to 5 weeks. She hurt the upper end of the forearm 3 months before admission and had had pain for 1 week. At that time she was seen in the hospital and showed, on physical examination, a bowing of the right humerus with two bulbous enlargements of middle and lower thirds of the shaft. There was no other deformity in any other portion of the skeleton; no asymmetry of the face. Roentgenograms were taken of the whole skeleton but have been discarded since. They were reported as negative except for the right humerus, right radius, and right thumb. A diagnosis of osteitis fibrosa cystica was made and at that time no special kind of treatment seemed to be indicated. At the age of 23 she returned with a fresh fracture of the right humerus at the junction of middle and lower thirds. She stated that in the meanwhile she had attended a course in nursing in Chicago. During this course she fell and fractured the shaft of the right radius. The arm was immobilized in a plaster cast, and the fracture healed within 4 weeks. Possibility of hyperparathyroidism was considered and the patient received four X-ray treatments to the neck region. She was in the best of health and without any symptoms from her right arm until she fractured the right humerus a day before admission. The fracture was set, and she was put in a shoulder spica. There was good callus formation in 6 weeks. Blood chemistry showed normal values (serum calcium 10.7 milligrams, phosphorus 3.4 milligrams, and phosphatase 5.4 milligrams).

Roentgenograms were taken of all bones of the body but pathological changes were found only in the right upper extremity, and here only the bones of the outer side were involved: humerus, radius, and bones of the thumb.

The humerus was considerably enlarged. The enlargement was mainly due to thickening, but there was also some real lengthening. Measurements of the roentgenograms showed the right humerus to be 15 inches long; the left being only 14 inches long. If one considered the existing lateral bowing of the right humerus, then the difference in length became even more marked. The upper and lower epiphyses of the right humerus showed perfectly normal shadow; the entire diaphysis, however, was altogether pathological. The cortical bone was thinned out very considerably, especially in the outer side, but in no place entirely interrupted. In some places it was difficult to speak of a real cortex. The bony shadow ended sharply toward the surrounding soft tissues. The periosteal surface was smooth; the diaphysis was remarkably thickened. The middle of the diaphysis was 2 inches in diameter versus ¾ inch on the normal, left, side. The bony structure can be called a diffuse osteoporosis with an even more marked degree in the lower half. There, one may even speak of a cystic area from the roentgenological point of view. Where the more solid bone tissue bordered at the cystic area, there one could still see two transverse lines of increased density, suggesting the places where previously pathological fractures or infractions had occurred. Bony trabeculæ could be made out on the inner concave side where they even showed a certain static arrangement, whereas most of the porotic areas appeared in a more diffuse cloudy shadow. The normal outline of the humerus spoke against active periosteal bone production, but one found at the upper third of the outer cortex definite signs of periosteal bone formation in form of a layer of porotic bone tissue at the surface of the old cortex.

The only bone of the forearm which was involved was the radius. The changes were very similar to those of the humerus, but not as extensive. The upper third appeared blown up to about twice its normal size. The cortex was markedly thinned out or had even disappeared entirely. Nevertheless, there was a sharp outline of the bony shadow everywhere. The bony structure of the upper third was again of the same hazy, cloudy structure without definite signs of bony trabeculation, but the whole area did not exactly give the impression of being cystic. The

cloudy shadow extended up in the head of the radius but, in the anteroposterior view, one found a narrowed zone of normal bone structure in the subchondral region. The proximal blown-up area was separated from another focus in the distal third by a kind of hour-glass constricture of ½ inch length, where the bony structure seemed to be more normal. The distal focus was almost 4 inches long, ¾ of an inch wide and rather sharply outlined, almost of cyst-like appearance. The cortex was thinned out, shell-like, but in no place interrupted. The distal epiphyses showed perfectly normal bony structure. There was no increase in the length of the radius.

All the carpal bones had normal bone shadows. The first metacarpal bone showed thickening with the same irregular, cloudy, bony shadow, eccentric atrophy of the cortex, and instead of the normal biconcave shape a diffuse bulging. The proximal epiphysis was of normal bony structure, the distal end, however, showed the same pathological structure as the diaphysis, which agreed very well with the absence of a distal epiphysis in the first metacarpal bone. Similar changes were also present in the first phalanx. Here, too, the proximal end was spared but the bony surface was increased in thickness. No definite changes were present in the distal phalanx.

This description was taken from plates which were sent us by courtesy from the X-ray Department of St. Luke's Hospital of Chicago. Pictures taken at re-admission to the hospital showed essentially the same changes, with a fresh transverse fracture through the middle of the diaphysis of the humerus.

From the roentgenological appearance there can be no doubt that Case 24 represents the same pathology as Case 23. The roentgenograms of the involved upper extremities are almost identical. The difference between both cases lies only in the fact that Case 24 showed involvement of the upper extremity alone whereas Case 23 revealed the same pathological changes in the left upper and lower extremities. Case 24 represented only a monomelic type of this unilateral lesion without any changes in the face. Monomelic changes without asymmetry of the face were also present in Case 25, which, with its involvement of only femur and tibia, forms a very welcome pendant to Case 24, the one representing the monomelic form of the upper, the other of the lower extremity.

CASE 25. Patient, a 22 year old woman, was admitted to the hospital for an appendectomy. She complained also of pain in the left hip of 18 years' duration. The pain was intermittent and when more severe, she was forced to limp. There was no history of trauma or fracture. On physical examination, a slight atrophy of the left lower extremity was found, but there was no difference in length. The leg was perfectly straight, but the femur showed diffuse bony enlargement and was tender on pressure. There was no soft tissue swelling. Blood chemistry normal (calcium 9.2 milligrams, phosphorus 3.3 milligrams). Roentgenograms disclosed pathological changes only in the left femur and tibia; all other bones of the skeleton were perfectly normal.

Left femur showed a very extensive involvement of the diaphysis, leading to a very irregular picture of hyperostotic porotic changes. Only a small portion of the lower third of the diaphysis was spared; all the epiphyses appeared in perfectly normal bony structure. This could be seen especially well at the junction of the neck of the femur with the head and greater trochanter. There was a sharply cut borderline between healthy and pathological bone tissue corresponding exactly to the site of the previous epiphyseal plates. The porotic changes led to complete removal of normal bony tissue with formation of a very coarse, porotic, bony structure with more circumscribed areas of increased osteoporosis of cyst-like appearance. These changes were associated with expansion of the bone so that in the upper half the left femur was twice the size of the right. The cortical bone showed irregular thinning out from within, frequently to a paper-thin shell of bone. Still, the outer surface of the femur remained smooth; there were no signs of more marked periosteal reaction, although the thickening of the shaft must have occurred by very slow periosteal bone proliferation. The inner structure could best be described as pseudocystic. There were no definite signs of fracture, but some coarser, reinforced transverse lines of bony trabeculation, especially at the junction of upper and middle thirds, were suggestive of callus formation. An irregular area of grape-like calcification was present at the junction of middle and lower thirds, where a calcified chondromatous mass could be considered. Otherwise, however, the picture was entirely different from that of skeletal chondroma.

From the anatomical distribution of the bone involvement in these 3 cases, it is quite evident that we deal with a multiosseous systemic affection of the skeleton. Pathological changes occur along certain rays. In the upper extremities only the humerus, radius, and bones of the thumb are affected. And, similarly, in the lower extremity, only the femur, tibia, and bones of the big toe are affected. All other bones are perfectly normal. Unilaterally, therefore, means not that all the bones of the affected extremity are involved, but also that even the involved bones do not show pathological structure in all their

portions. Very characteristically, the epiphyses are constantly spared and the diaphyses show variable degrees of extension of the pathological changes. This is also true after the bone growth has stopped and the epiphyseal disc has disappeared, as shown in Cases 24 and 25, both about 22 years old. One has, therefore, to conclude that we deal here with a purely diaphyseal pathology, evidently with disturbance of the endosteal bone formation and without participation of the periosteum. There is nothing to suggest a disturbance of the enchondral ossification. The bone production at the epiphyseal discs seems to occur quite normally. It even appears that there is increase in length growth, probably due to the hyperemia of the bone marrow of tibia and fibula. This could also be observed in Case 20, which showed multiple involvement. Pathological changes seem to become manifest with the so called "internal molding resorption" which removes the primary spongy bone, replacing it with mature lamellar bone of static arrangement, in normal cases. In the affected bones of the 3 unilateral cases, however, the internal molding resorption, for some unknown reason, instead of leading to the formation of lamellar bone produces fibrous bone marrow with fibrous porotic spongy bone. The process is evidently of very long duration and only of slow progress. In all the cases it started apparently in early childhood and gradually involved the diaphyses. From the roentgenograms of the tibia of Case 25, it appears that the pathological changes in the affected bones do not develop from one center with gradual involvement of the surrounding healthy bone, but they start apparently simultaneously in different foci which first are separated but may merge later and give the picture of a diffuse involvement.

In the article referred to an attempt was made to define the term of osteodystrophia fibrosa unilateralis as well as possible and to rule out certain other bone diseases with which it has a number of symptoms in common. Especially Ollier's dyschondroplasia had to be ruled out because of the unilaterality of the disease and the asymmetry of the face. Ollier's disease, however, represents an intrinsic disturbance of enchondral ossification with formation of chondroma-like tumor masses at the site of the metaphyses. It is observed within the first year of life and usually leads to marked deformity and shortening of the affected extremities. In our cases clinical symptoms did not develop until after the fourth year of life in Case 25, the fifth year in Case 23, and the eighth year in Case 24. Real shortening as in Ollier's disease could not be observed. On the contrary, the involved bones in 2 cases tended to increase in length, and there was a real lengthening if secondary more marked bowing of the softened bones did not occur. Besides this, the roentgenological appearance of the affected bones was altogether different from that in Ollier's disease. They lacked entirely the coarse structure in the metaphyses with the characteristic club-like enlargement. They showed a more or less extensive involvement of the diaphyses only, with changes which best can be described as hyperostotic-porotic without participation of the periosteum. Against Ollier's disease spoke also the absence of cartilaginous tissue in the piece of tibia removed from Case 23.

On the basis of the findings in Cases 24 and 25, another systemic skeletal lesion has to be considered from the differential diagnostic viewpoint, and this is the melorheostose Léri. This was not done in our first article because of the unilaterality of Case 23, all the cases of melorheostosis showing only involvement of one extremity in which a number of bones (never all) become changed in a very peculiar way. Léri compared the appearance of the involved bones very adequately with the flow of the melted wax along the surface of a candle. There is, similarly as in our cases, a certain ray distribution of the pathological process; the flow, for instance, starting with the scapula, running down the humerus, radius, thumb, or third finger. By the way of distribution and by its monomelic appearance, melorheostosis has certainly a strong resemblance to our Case 24. This differs, however, quite considerably because of a number of other symptoms. Melorheostosis, as a rule, affects male adults. The average age of a great number of cases reported in the literature is 15½ years. The roentgenological

appearance is very typical, consisting in an osteosclerotic process which affects epiphysis as well as diaphysis, endosteal bone as well as periosteal bone, leading especially by the latter to the irregular thickening of the bones with drop-like prominences on the periosteal surfaces. Our 2 cases were both very young girls when the process started and the X-ray picture is characterized by the hyperostotic porotic change, which means that the affected bones show cloudy shadows (porosis) with diffuse or spindle shaped widening (hyperostosis). So, despite the monomelic affection and peculiar systemic anatomical distribution, melorheostosis can safely be ruled out.

RELATION OF OSTEODYSTROPHIA FIBROSA UNILATERALIS TO COMMON OSTEITIS FIBROSA

Remains the discussion of the relation of osteodystrophia (osteitis) fibrosa unilateralis to the more common type of osteitis fibrosa cases. They have in common the histological findings. We have, however, in our previous article stressed the point that the histological picture of osteitis fibrosa cannot be taken as a specific reaction of the bone marrow. We know that the same changes may occur under quite different stimuli and so the histological diagnosis of osteitis fibrosa may frequently be misleading and obscuring. In both of our cases, however, certain roentgenological signs, especially the apparent cyst formation, led to the first clinical diagnosis of cystic osteitis fibrosa. In Case 23 at time of first admission only X-ray pictures of the pelvis were taken (all the clinical symptoms pointed to the left hip), and so the diagnosis is quite justifiable. In Case 24 pictures were taken of all the bones of the body and a multiple "cystic" lesion was recognized. The extensive involvement of the bones, of course, speaks primarily and decidedly against a localized lesion of osteitis fibrosa. The multiple bones affected suggested generalized osteitis fibrosa in the sense of von Recklinghausen's disease or hyperparathyroidism, although the systemic distribution with unilateral or monomelic manifestation speaks *a priori* against a central cause. Blood chemistry in all 3 cases was essentially negative, especially as far as the calcium and phosphorus values were concerned. Nevertheless, in Case 23, an exploratory operation of the parathyroid glands was performed, two glands being removed with perfectly normal microscopic and macroscopic appearance. In Case 24 the neck region was irradiated with X-ray without any changes in the skeleton.

It is quite certain that both cases have essentially nothing to do with generalized osteitis fibrosa. Against it speaks the *age* (Recklinghausen's disease is not observed in childhood); *the roentgenological appearance* (Recklinghausen's disease leads to marked general osteoporosis of the skeleton with cyst formation and brown tumors; hyperostotic changes take place only at the site of pathological fracture; our cases showed very characteristic hyperostotic porotic changes with systemic unilateral or monomelic distribution. There were no definite signs of real cyst formation); and, finally, *the normal clinical findings with absence of general symptoms.*

Thus, it seems that osteodystrophia fibrosa unilateralis deserves an independent position among the osteitis fibrosa cases. And, as a matter of fact, this was also the conclusion in the paper referred to. However, since the observation of Cases 24 and 25, which can be considered as less extensive unilateral cases, it is theoretically possible to assume that there are different degrees in extension of fibrous osteodystrophy. One could think that in the same way as Cases 24 and 25, monomelic distribution represents a reduction of a strictly unilateral manifestation, the extensive monosseous cases represent less extensive degrees of monomelic forms and, finally that the localized lesion could be considered as the mildest form in the development of fibrous osteodystrophy. Case 25 especially, with the changes in the tibia just in the beginning and the bones of the foot perfectly free, is a very welcome link in the chain of different manifestations of fibrous osteodystrophy. It stays between the monomelic case (Case 24) and the monosseous diffuse form (Cases 21 and 22). Such an assumption is, of course, very hard to prove, since we know so little about the etiology of fibrous osteodystrophy. But it does not seem entirely artificial if one considers the very marked regularity in the distribution of our 2 cases in which, as far as the

upper extremities are concerned, the lesions resemble each other like one egg another. Furthermore, the typical localizations of the localized monosseous type would also fit very well in this conception of a primary endosteum lesion. It really must be quite surprising to find the upper metaphysis of the humerus, femur, and tibia so often involved without thinking of a certain intrinsic predisposition of these portions to fibrous osteodystrophy. It is always a metaphyseal or diaphyseal lesion without primary participation of the periosteum. Even after disappearance of the epiphyseal plates, the borderline between epiphysis and diaphysis remains strictly observed. It is a disturbance of endosteal bone formation in the diaphysis which starts apparently most frequently in the juxta-epiphyseal portions where the primary spongy bone in normal cases is transformed to mature lamellar bone tissue. Of what kind this disturbance is, if the simple traumatic factor is unable to solve the problem, it is impossible to say with our present knowledge of bone formation and bone growth. It has to be admitted that trauma may facilitate the development of such a lesion, but it cannot be the real etiological factor. To our knowledge, all the experiments undertaken to cause localized osteitis fibrosa by trauma and intermedullary trauma have failed. In most of the clinical cases the onset is insidious and, when fractures occur, they are, as a rule, pathological, developing in the diseased and weakened skeletal portions. All the cases have in common the relatively benign clinical course which in the localized cases may lead even to spontaneous healing. The more extensive cases are, of course, not as favorable as far as prognosis is concerned; they even resist quite often radical surgical procedures, showing marked tendency to recurrence. The unilateral cases, however, are at present entirely inaccessible for treatment, except for a symptomatic one in cases of complications.

Summarizing, we can say for the group of osteitis fibrosa: There are localized cases of a solid or cystic type, usually situated in the upper portion of the diaphysis of the humerus, femur, and tibia; less frequently, diaphyseal localization is observed; never localization in epiphyses. Besides the localized form, more extensive cases can occasionally be seen with involvement of the greater part of the diaphyses. Multiple localized lesions are rare but may occur without any apparent rule in the distribution of the lesion. There is a strictly unilateral (monomelic) form of fibrous osteodystrophy with involvement of the entire or of great portions of the diaphyses of bones arranged in longitudinal ray-like anatomical distribution. On the basis of such observations, it is believed that the localized form represents an abortive type of the extensive monosseous form. The latter is an abortive form of the monomelic type which, in turn, is considered as an abortive form of the unilateral osteodystrophy. Inasmuch as the latter cannot be taken as traumatic in origin, the purely traumatic etiology of all the other forms is rather doubtful. All the cases mentioned have apparently no nosological relationship to the generalized form of osteitis fibrosa. Von Recklinghausen's disease has to be considered as a generalized bone disease in which every part of the skeleton is affected. The degree of affection may vary, according to mechanic irritative factors. The distribution of cysts and brown tumors in the generalized form is irregular and does not follow certain rules. Disturbance of calcium metabolism and tumor formation in parathyroid glands is demonstrable almost in every case of von Recklinghausen's disease, never in the different "localized" forms of fibrous osteodystrophy.

THE RELATION OF CHRONIC MASTITIS TO CERTAIN HORMONES OF THE OVARY AND PITUITARY AND TO COINCIDENT GYNECOLOGICAL LESIONS

PART II—CLINICAL AND HORMONE STUDIES[1]

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THE first part of this study which appeared in a previous number of this journal was concerned with a consideration of possible causes and the histology of the diffuse breast diseases commonly classed under the general term of "chronic mastitis." Particular attention was devoted to the current belief in an underlying ovarian dysfunction and to an alternative theory giving nervous and vascular factors a more prominent rôle. The present paper is a continuation of this work and consists in a collection of clinical and laboratory evidence having a bearing on these two conceptions.

The clinical data for the study of chronic mastitis are based upon 261 cases of diffuse breast disease observed during the 3 year period of 1931–1933 inclusive. Of these 239 were primarily patients of the breast clinic at the Memorial Hospital, whereas, 22 were from the gynecological department of the Roosevelt Hospital.

CLASSIFICATION

The original 261 cases have been divided first into three groups based upon the clinical character of the disease in the breast. The histological basis of these clinical forms has already been discussed. (1) In the first group were placed the 183 cases with tender areas of induration or nodularity. Among these patients were many who complained of a temporary premenstrual swelling but none with permanent enlargement or discharge from the nipple. (2) The second group consisted of 31 patients, all of whom reported a permanent enlargement of the breasts, usually with cyclical pain and swelling, but without discharge from the nipple. (3) The third group of 47 cases was made up of the patients with discharge from the nipple, which necessarily included many with pain and 6 with hypertrophy.

A secondary classification based on a gynecological history and examination was made to bring out the importance of the two major theoretical etiological factors, ovarian dysfunction and a nervous and vascular disturbance perhaps caused by or associated with pelvic lesions. Since the endocrine factor is more in harmony with present views, the groups given below are arranged in order of the apparent prominence of glandular dysfunction. The incidence of lesions having a possible effect on the pelvic nerves is found in the data on inflammation, parametritis, retroversion, and cervical infections.

The classification which has been employed is as follows:

1. Breast disease in association with cystic ovaries and menstrual abnormalities (anatomical and functional evidence of ovarian disorder).

2. Breast disease in association with cystic ovaries but normal menstruation (anatomical evidence only of ovarian disorder).

3. Breast disease without evidence of anatomical disease of the ovaries, but with menstrual abnormalities (functional evidence only of ovarian disorder).

a. Prolonged menstrual cycle, 35 days or longer.

b. Scant menstrual flow, 2 days or less.

c. Excessive or prolonged flow, 8 days or more.

d. Short menstrual cycle, 21 days or shorter.

4. Breast disease following hysterectomy (functional disturbance of retained ovaries).

5. Breast disease without evidence of cystic ovaries or menstrual abnormalities but with signs of inflammation or pelvic congestion (no clinical evidence of ovarian disorder).

a. Acute and chronic salpingo-oophoritis.

[1]This work has been aided by a grant from the Egbert C. Fuller Fund.

TABLE I.—CLINICAL CLASSIFICATION OF 183 CASES WITH BREAST PAIN WITH NODULARITY

	Total	Age	Marital Status				Menstrual Cycle							Duration of Flow			Uterus						Parametria		Adnexa					Cervix				Thyroid	
		Average age in years	Single	Married. No pregnancies	Miscarriages only	One or more children	Normal	Long cycle. 35 days or more	Short cycle. 23 days or less	Irregular. 21–35 days	Continuous	Amenorrhea		Normal duration	Short menses. <3 days	Long menses. >7 days	Normal	Retroversion. 1st degree	Retroversion. 2nd degree	Retroversion. 3rd degree	Partial prolapse	Fibroids	Normal	Tenderness: dyspareunia	Normal	Acute salpingo-oophoritis	Chronic salpingo-oophoritis	Previous salpingo-oophoritis	Cystic ovaries	Prev. removal cystic ovary	Normal	Laceration	Erosion	Endocervicitis	Hypertrophy	No pelvic examination
1. Cystic ovaries and abnormal menses	11	29	2	2	0	7	5	1	4	1				1	7	3	3	2	2	4		2	9	2			6		9	2		1	4	1	1	
2. Cystic ovaries and normal menses	18	31	2	4	2	10	18							18			6	2	1	6	3	3	13	5		3	3		16	2	2	0	8	4		
3. Abnormal menses but no demonstrable cystic ovaries																																				
a. Long cycles	23	32	5	3	4	11		18		5				18	4	1	11	3	2	3		2	18	3	20		1				3	3	2	4	1	2
b. Short flow	20	33	4	2	0	14	18		2						20		2	4	5	3	3		12	5	17						7	4	3	2	1	3
c. Excessive flow	5	39	1	3	0	1	3				2					5	5					3	5	0	5								1			
d. Short cycles	15	33	1	3	0	11			15					15			4	3	5	2			7	7	13		1				4	2	4	1		1
4. Posthysterectomy	2	32				2						2											2		2						1					
5. Normal menses with pelvic inflammation or congestion																																				
a. Pelvic inflammation	9	32	0	4	2	3	9							9			4	4	1	0	0	2	6	3		1	6	2			3			2	1	
b. Pelvic congestion: parametritis	24	32	1	3	2	18	24							24			10	6	6	2	2	4		24	24						5	5	9	4	1	
c. Retroversion	17	34	1	3	0	13	17							17			0	0	7	9	1		17		17						2	7	5	1	2	
d. Cervical infections	8	30		2		6	8							8			5	3					8		8							4	1	3		
e. Sexual factor only	3	33	1	1		1	3							3			1	1					2		2						2				1	1
6. Primary dysmenorrhea	12	25	11	1			12							12			3	1				1	4		4						3				2	8
7. Thyroid hypertrophy	4	29	1	1		2	4							4			1	2					3		3						3				4	1
8. Unclassified	12	30	6			6	12							12			5	4				1	9		9						6					3
Total	183	30.7	36	33	9	105	133	19	21	6	2	2		141	31	9	60	35	29	29	9	18	115	49	124	4	17	2	26	4	41	26	37	21	14	19

b. Chronic parametritis and pelvic congestion.

c. Retroversion and partial prolapse.

d. Cervical infection and hypersecretion.

e. Presence of an apparent sexual relationship.

6. Breast disease with primary dysmenorrhea.

7. Breast disease with thyroid hypertrophy.

8. Unclassifiable cases.

The first four groups contain all the cases in which there were clinical signs or symptoms suggestive of an ovarian dysfunction. Group 5 includes cases without evidence of an ovarian dysfunction but with lesions in the pelvis, making an irritation of the pelvic sympathetic nerves a possibility. A number of cases with such pelvic disease showed also evidence of ovarian abnormality and have been arbitrarily classed in the dysfunction groups. The total incidence of pelvic lesions can therefore be obtained only by reference to the detailed tabulation in the charts (Tables I, II, III). Cases with no classifying feature except pri-

TABLE II.—CLINICAL CLASSIFICATION OF 31 CASES WITH HYPERTROPHY OF THE BREAST

	Total	Age	Marital Status				Menstrual cycle						Duration of Flow			Uterus					Parametria		Adnexa				Cervix			Thyroid	
		Average age in years	Single	Married. No pregnancies	Miscarriages only	One or more children	Normal	Long cycle. 35 days or more	Short cycle. 23 days or less	Irregular. 21–35 days	Continuous	Amenorrhea	Normal duration	Short menses. <3 days	Long menses. >7 days	Normal	Retroversion. 1st degree	Retroversion. 2nd degree	Retroversion. 3rd degree	Partial prolapse	Fibroids	Normal	Tenderness: dyspareunia	Normal	Acute salpingo-oophoritis	Chronic salpingo-oophoritis	Previous salpingo-oophoritis	Cystic ovaries	Prev. removal cystic ovary	Normal	Laceration	Erosion	Endocervicitis	Hypertrophy	No pelvic examination
1. Cystic ovaries and abnormal menses	3	30		2	1		1	2					1	2		3					3				1		3				1		
2. Cystic ovaries and normal menses	3	28	1			2	3						3			3				2	2	1					2	1					
3. Abnormal menses but no demonstrable cystic ovaries																																	
a. Long cycles	4	20	2	1		1		4					4			2					2		2						1	1			2
b. Short flow	2	23	1	1			2							2		1	1				2		2							1			
c. Excessive flow	1	44				1	1								1			1			1		1						1				
d. Short cycles																																	
4. Posthysterectomy	6	37	1	1	1	3						6									6		6					2	2				
5. Normal menses with pelvic inflammation or congestion																																	
a. Pelvic inflammation																																	
b. Pelvic congestion: parametritis	4	30		2		2	4						4			2	1	1		1		4	4						1		1	2		
c. Retroversion	1	39		1			1						1					1			1		1						1				
d. Cervical infections																																	
e. Sexual factor only	3	25	1	2			3						3			3					3		3						3				
6. Primary dysmenorrhea	3	25	3				3						3			1					1		1						1				2
7. Thyroid hypertrophy	1	25	1				1						1																				1
8. Unclassified																																	
Total	31	29.1	10	10	2	9	19	6				6	20	4	1	15	2	3		3	21	5	20		1		5	3	9	1	3	3		5

mary dysmenorrhea or thyroid hypertrophy have been separately grouped since these conditions may have either an endocrine or nervous significance.

METHODS OF HORMONE STUDY

As patients were admitted to the clinic, typical examples were selected for hormone studies, based on four types of analysis:

1. *The urinary excretion of estrin.* Estrin was obtained from the urine by the chloroform extraction method of Frank (15) and assayed by injection of the extract in oil into spayed adult white mice. In all except the earlier determinations, a positive reading was accepted only when full estrus occurred in three of four animals injected with the same quantity of hormone according to the plan of Siebke (53). On account of the variation in excretion at different times in the monthly cycle, the total estrin excreted during a menstrual cycle was determined by the separate assay of consecutive 72 hour total urine specimens.

TABLE III.—CLINICAL CLASSIFICATION OF 47 CASES WITH ABNORMAL SECRETION FROM THE NIPPLE

	Total	Age	Marital status				Menstrual cycle						Duration of flow			Uterus						Parametria		Adnexa					Cervix				Thyroid	
		Average age in years	Single	Married. No pregnancies	Miscarriages only	One or more children	Normal	Long cycle. 35 days or more	Short cycle. 23 days or less	Irregular. 21–35 days	Continuous	Amenorrhea	Normal duration	Short menses. <3 days	Long menses. >7 days	Normal	Retroversion. 1st degree	Retroversion. 2nd degree	Retroversion. 3rd degree	Partial prolapse	Fibroids	Normal	Tenderness: dyspareunia	Normal	Acute salpingo-oophoritis	Chronic salpingo-oophoritis	Previous salpingo-oophoritis	Cystic ovaries	Prev. removal of cystic ovary	Normal	Laceration	Erosion	Endocervicitis	Hypertrophy	No pelvic examination
1. Cystic ovaries and abnormal menses	5	33			1	4		3	2				1	2	2	1		1	2		2	3	2			1		5		1	1	1	1		
2. Cystic ovaries and normal menses	3	36				3	3						3						3			3							3	1	1			
3. Abnormal menses but no demonstrable cystic ovaries																																		
a. Long cycles	13	39	1	2	0	10		12		1			8	4	1	6	4	1		2	10	1	11						8			2		2
b. Short flow	3	32				3	3							3		1		2			1	2	3							2			
c. Excessive flow	1	42				1			1						1	1				1	1		1							1			
d. Short cycles	6	35	1	1		4			6				6			1	4	1			4	2	5		1				1	2	1	1		
4. Posthysterectomy	5	39	1		1	3						5									5		5					2	3		1		
5. Normal menses with pelvic inflam. or congestion																																		
a. Pelvic inflammation	1	31				1	1						1			1					1			1								1		
b. Pelvic congestion-parametritis	1	28				1	1						1					1				1	1									1		
c. Retroversion	5	32		1		4	5						5					2	3		5		5							2	1	1		
d. Cervical infections	3	34				3	3						3			3				1	3		3								2	1		
e. Sexual factor only																																		
6. Primary dysmenorrhea																																		
7. Thyroid hypertrophy																																		
8. Unclassified	1	25	1				1						1																					1
Total	47	35.6	4	4	2	37	17	15	9	1		5	29	9	4	13	5	11	9	1	6	36	8	34	1	2		5	5	14	9	6	8		3

The normal excretion of estrin during a single cycle was found by Frank (15) to vary from 800 to 1,500 mouse units, by Siebke (51) from 200 to 2,000. A peak of excretion near the time of ovulation was noted by both of these workers and a second peak shortly before menstruation by Frank (15). Control tests made upon 4 normal women in the course of this study gave a range of 760 to 2,625 and an average of 1,505 mouse units. The study of the patient with the highest output was completely repeated after a 6 months' interval, the second determination showing 3,155 units. The highest rates of excretion were found near the middle of the month, but occasional unexplained peaks occurred at other times.

On account of the many types of menstrual disturbance reported in cases of chronic mastitis, it is important to reconsider the variations in hormone excretion that have already been reported in relation to these menstrual abnormalities. Menstrual cycles of increased

length may according to Siebke (54) be of two kinds, those with a period of complete rest preceding the beginning of the usual hormone cycle and those with a continuous hormone excretion, possibly with several peaks, during the entire interval. Amenorrhea similarly may be of several types (Frank and Goldberger, 16), varying from the practical absence of hormone in blood and urine to the excessively high levels reported in the so called polyhormonal amenorrhea of Zondek (60). The hormone basis for the short cycle has been little studied. The variability of amount and duration of the menstrual flow within relatively normal limits is not, according to Siebke's (52) observations, dependent upon quantitative variations in the ovarian function.

2. Blood estrin. The test of Frank and Goldberger (17) for the female sex hormone was employed for study of the presence of the hormone in the blood. The originators of the test maintain that a positive reaction, as a rule, may be obtained in normal women during the premenstrual week. This has been both corroborated (Hirsch; Siebke, 51; Mazer and Andrussier), and contradicted (Janney, Ford and Mueller). Experience with a short control series has shown that in our hands negative tests are not infrequently obtained during the premenstrual week, a point to be remembered in interpreting the results given below. In a few recent cases the test of Fluhmann (11) based on the production of mucification of the vaginal mucosa of the spayed mouse has also been used.

An increase of follicular hormone in the blood has been observed in certain types of bleeding at puberty and the menopause (Frank and Goldberger, 16; and Siebke, 52). High values have been found also in certain cases characterized by premenstrual nervous tension in which various vascular and nervous symptoms are prominent, and dysmenorrhea with breast pain and swelling may be present (Frank, 14). Low values have been found in some women with functional sterility but normal menstrual cycles (Frank, 14; Mazer and Andrussier).

3. The urinary excretion of prolan. Attempts were made to demonstrate the presence of prolan in the urine by the use of the alcohol precipitation method of Zondek (62) and the benzoic and tungstic acid methods of Katzman and Doisy (27, 29). Extracts by the two latter methods were prepared by, and under the direction of, Dr. Helen Downes of the department of chemistry of the hospital. These tests also were carried out upon a series of urines obtained at 3 day intervals throughout the menstrual cycle.

Previous estimations of the daily prolan output of normal women have varied widely. Zondek (64) reported 8 units per day in the postmenstruum, 25 in the interval, 29 in the premenstruum, and 25 during menstruation. Katzman and Doisy (28, 29) found a maximum excretion of 12 to 16 mouse units at about the time of ovulation and sometimes a rise during menstruation, with the amounts between these times falling to three mouse units, one rat unit, or less. Other workers have reported only traces of prolan in the urine of normal women.

These conflicting results are undoubtedly due to variations in technique. One of the most important is found in the particular physiological reaction taken as the measure of a unit, there being two commonly employed. These are, first, the direct effect on the ovarian follicle; second, the indirect effect on the tubular tract, in particular the opening of the vaginal introitus and the production of the estrus type of vaginal spread. The latter appears more reliable but undoubtedly requires much more hormone than is needed to produce slight follicular changes.

Tests on the urine of normal women with extracts concentrated to show from 5 to 20 units of prolan per liter when injected into infantile mice were found by us rarely to produce opening of the introitus and never full estrus. Evidence of partial ripening of the follicles was frequently present in the serial sections of the ovaries but was difficult to evaluate for comparative purposes.

A great increase of prolan excretion has been found in the presence of certain malignant tumors, such as chorionepithelioma and teratoma, and a slight increase has been reported in the presence of other new growths especially those of the female genital organs

TABLE IV.—REPRODUCTIVE HISTORY

	Cases with pain	Cases with hypertrophy	Cases with secretion
	183	31	47
	Per cent	Per cent	Per cent
Single women	19.2	32.3	8.5
Married—childless	17.5	32.3	8.5
Miscarriage only	4.9	6.5	4.3
One or more children	57.9	29.0	78.7

TABLE V.—MENSTRUAL DISTURBANCES

	Cases with pain	Cases with hypertrophy	Cases with secretion
	183	31	47
	Per cent	Per cent	Per cent
Normal menstruation	58.5	48.1	29.7
Amenorrhea after hysterectomy	1.1	19.4	10.7
Abnormal menstruation	40.4	32.2	59.6

(Zondek, 63; Hamburger). Besides these neoplastic conditions, an increase in prolan excretion occurs in women with marked degrees of ovarian deficiency, particularly in the menopause (Zondek, 61, 62; Oesterreicher; Lassen and Brandstrup). In the amenorrheas of long standing in young women, the hormone has been occasionally found (Zondek, 60; Kaufmann and Muehlbock), but in the milder forms of ovarian hypofunction its presence has not been proved. Besides these ovarian conditions, prolan has been reported in cases with certain diseases of the central nervous system (Kraus) and migraine (Riley, Brickner, and Kurzrok). These points are of importance on account of the delayed and scant menstruation and headaches (Whitehouse) noted in cases of the painful breast.

4. Serum prolan. The test of Fluhmann (10), consisting of the simple injection of small amounts of blood serum into infantile mice is capable of demonstrating prolan when it is present in relatively large amounts in the blood stream. Blood from normal women never produces a vaginal reaction, although possible follicular changes may be observed. This test was likewise applied to a series of mastitis patients at weekly intervals. Fluhmann (10) found prolan A in the blood of certain patients with prolonged amenorrhea, but obtained negative results in women suffering from the minor degrees of hypo-ovarianism, as manifested by persistently delayed menses, scanty menses, and short periods of amenorrhea.

5. Examination of the endometrium. The uterine mucosa of any patient is an extremely sensitive indicator of her ovarian function, subject to none of the indirectness or loss inherent in any method involving extraction and reinjection. For that reason the evidence afforded by examination of endometrium from 31 cases of breast disease is especially important.

RESULTS OF THE CLINICAL AND HORMONE STUDY

The evidence having a bearing on the etiology of chronic mastitis has been assembled under thirteen headings.

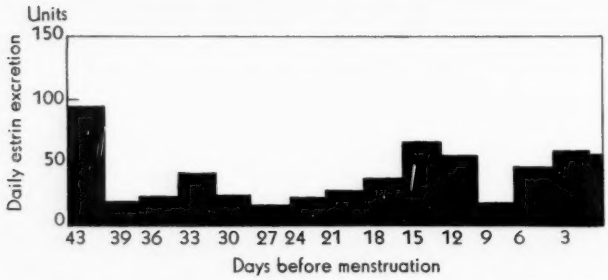
1. Age incidence. The average age of the patients with pain was 30.7 years, those with hypertrophy 29.1 years, and those with secretion 35.6 years.

2. Reproductive history (Table IV). A contrast is afforded here between the cases with hypertrophy, nearly two-thirds of which were childless, and those with secretion, the great majority of whom had borne children.

3. Menstrual history. The frequency of menstrual disturbance in cases of chronic mastitis has heretofore been the chief clinical evidence of an ovarian dysfunction. The total incidence of abnormalities in the frequency or duration of the menstruation is shown in Table V.

a. Disturbances in the cycle of menstruation (Table VI) were most common in the cases with discharge from the nipple and were usually of the delayed period or prolonged interval type.

The daily excretion of estrin in the long cycle cases of this study averaged less than those with a regular rhythm (Tables IX A, IX B, IX C, IX D), but Zondek (60) in particular has reported the reverse in the so called polyhormonal amenorrhea in which there may be breast symptoms. An example of the estrin



Graph 1. Total estrin excretion in the 43 day cycle of a patient with non-puerperal secretion from the nipples. Exp. 166. Total units 1,743.

excretion in the prolonged cycle type is shown in graph 1, obtained from the following case:

CASE 1. S. W. Patient was admitted to hospital February 16, 1934. She was 34 years of age, married and had two children, ages 7 and 3½ years. Menstruation had always occurred at 6 to 8 week intervals with a 5 day, normal flow and no dysmenorrhea. No discomfort had ever been felt in the breasts until 2 weeks before admission when a discharge was noted from the left nipple. Examination showed the breasts medium in size, dependent in shape, with wide slightly congested areolæ, and a moderate diffuse nodularity in both outer quadrants. A little oily discharge could be expressed from the left nipple, and at a later visit some was obtained from the right also. By vaginal examination, the fundus was found slightly retroverted and enlarged with a moderately hypertrophied and eroded cervix and a slight enlargement of the right ovary.

Hormone tests: The excretion of estrin amounted to 1,743 mouse units in 43 days. Three blood serum specimens tested by the Fluhmann method for estrin were negative. No increase in prolan was found in 3 serum specimens or in 14 specimens of urine extracted by the tungstic acid procedure of Katzman and Doisy.

TABLE VI.—DISTURBANCES IN THE CYCLE OF MENSTRUATION

	Cases with pain	Cases with hypertrophy	Cases with secretion
	183	31	47
	Per cent	Per cent	Per cent
Normal cycle	72.7	61.3	36.2
Amenorrhea after hysterectomy	1.1	19.4	10.6
Long cycle—35 or more days	10.4	19.4	31.9
Irregular cycle—21 to 35 days	3.3	0	2.1
Short cycle—21 or fewer days	11.5	0	19.2
Continuous bleeding	1.1	0	0

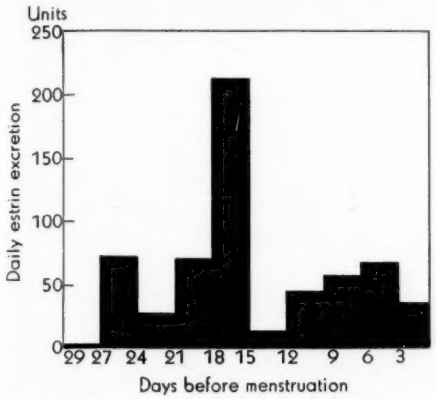
b. Disturbances in the duration of the menstrual flow (Table VII). A decrease in the amount of the menstrual flow in the cases of painful breast has been described repeatedly and was noted in 16.9 per cent of the patients of this series. It was also common with secretion from the nipple.

Since the scant periods have been cited as evidence of an underfunction of the ovary, it is interesting to note that the monthly estrin excretion in 6 women with periods of less than 3 days was not below the general average (Table IX B, IX C). An example of the estrin excretion in a woman, menstruating for only 1 day, is shown in Graph 2. The history of this case follows:

CASE 2. T. J. Patient was admitted to hospital February 2, 1932. She was married, age 26 years, with a history of one normal delivery, 2½ years, and a therapeutic abortion 1 year, before admission. Menstruation had formerly been of the type, 28, 3½, average, without pain, but since the birth of her child the periods had gradually been reduced to a very scant flow of 1 day's duration and become associated with headache, dizziness, and dysmenorrhea.

Three months after the delivery of her child her left breast had been removed by radical mastectomy for carcinoma. For 3 months before her admission to the Memorial clinic there had been marked pain in the right breast, chiefly premenstrual, with hypersensitivity of the skin of the axilla, right shoulder, and arm, and occasionally of the right leg. In addition there was some weakness of the right hand, with general nervousness, anxiety, headache, and dyspareunia.

Examination showed the right breast small, dependent, and slightly nodular in the outer quadrants. The uterus was normal in size, in midposition, with tenderness elicited by its motion. The adnexa were tender and the cervix large.



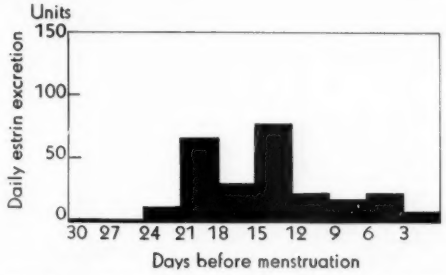
Graph 2. Total estrin excretion in the 29 day cycle of a patient with painful breasts and a menstrual flow of 1 day. Exp. 103. Total units 1,756.

The case was treated for 4 months with theelin without success and then selected for hormone study. No abnormalities were noted in the prolan or estrin content of either blood or urine.

Hormone tests: The excretion of estrin amounted to 1,756 mouse units in 29 days. Four blood tests (Frank and Goldberger, 17) gave a single positive reaction in the third week. There was no evidence of increase in prolan in 3 specimens of serum or in 9 of urine extracted by the tungstic acid method.

Diminished menstruation cannot therefore be accepted as necessarily a sign of ovarian underfunction and may be dependent on a local pelvic or uterine abnormality. The dyspareunia and pelvic pain in this case will recall the fact noted in the first section of this paper that a diminishing menstruation has been ascribed to a chronic parametritis.

c. The appearance of breast symptoms after hysterectomy was noted in 12 cases. In all of these there was satisfactory evidence that one or both ovaries had been retained, and in the urine of all cases studied estrin was demonstrable. An example of the cycle of estrin excretion after hysterectomy is shown in Graph 3.



Graph 3. Total estrin excretion during 30 days in a patient with breasts painful following hysterectomy. Exp. 155. Total units 762.

CASE 3. K. Patient was admitted to hospital September 11, 1931. She was married, 35 years of age, with two children, ages 12 and 2 years, and a history of one miscarriage 5 years before admission. The symptoms at first consisted in irregular uterine bleeding and a lump in the right breast. During the following 3 years the patient underwent four operations: a myomectomy, the excision of a fibroadenoma, a curettage, and finally a supravaginal hysterectomy. The ovaries were noted as normal at the last operation, although no special attention was given them by the surgeon.

Following her operation, the patient noted an increase in pain and swelling of her breasts, symptoms which appeared to undergo cycles of exacerbation. Examination of the breasts 11 months after the operation showed them to be nodular in their outer quadrants.

Hormone tests: The excretion of estrin amounted to 762 mouse units in 30 days. Four blood serum specimens tested by the Fluhmann technique gave one weak reaction. No definite increase in prolan was found in 4 serum specimens or in 10 specimens of urine extracted by the tungstic acid method.

TABLE VII.—DISTURBANCE IN THE DURATION OF THE MENSTRUAL FLOW

	Cases with pain	Cases with hypertrophy	Cases with secretion
	183	31	47
	Per cent	Per cent	Per cent
Normal flow	77.1	64.5	61.7
Amenorrhea after hysterectomy	1.1	19.4	10.6
Short flow—less than 3 days	16.9	12.6	19.1
Long flow—more than 7 days	4.9	3.2	8.5

TABLE VIII.—OVARIAN CONDITIONS OBSERVED AT OPERATION

	Cases with pain	Cases with hypertrophy	Cases with secretion
Follicle cysts	19	4	6
Cystic corpora lutea	3	0	3
Salpingo-oophoritis	4	0	1
Miscellaneous	9	3	2
Normal	8	3	3

Fig. 1. SC8597. Follicle cysts and papillomas of the ovary in a case with pain and swelling of the breasts and secretion from the nipples.

Besides these benign cases, 11 instances of breast cancer following hysterectomy have been observed by the writer during the last 5 years, although no systematic search of the hospital files has been made. It is of incidental interest that Aschner maintains that a special tendency to cancer exists in the breasts of women who have had their uterus removed and includes this danger among his reasons for preferring myomectomy to hysterectomy for the treatment of uterine fibroids.

The reason for the development of breast disease after hysterectomy is not clear. An ovarian dysfunction based on cystic changes developing in the retained ovary, is a possibility, although recent experimental work has not strengthened the accepted clinical belief in such a process (Sessums and Murphy). One study, that of Kosakaé, Ohga and Okamoto, has reported an increase in estrin excretion after hysterectomy, perhaps due to the failure of the endometrium to utilize its quota of hormone. In 2 cases completely studied by us, no increase in estrin excretion was found, although high values were obtained in a third patient from whom, however, only a series of 8 discontinuous 24 hour specimens could be procured. It must finally be pointed out that the pelvic plexus of sympathetic nerves must unquestionably be affected by the removal of the uterus and the subsequent inflammatory and reparative processes. The sudden appearance of milk shortly after supravaginal hysterectomy with preservation of an ovary suggests therefore the possibility of a nervous as well as an endocrine factor in the following case.

TABLE IX A.—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 5 NORMAL WOMEN

Experiment number	Menstruation	Pelvic pathology	Mouse units
9	30.4	Normal	760
13	30.5	Normal A	2625
112. Repeat 13	30.5	Normal B	3155
59	30.3–4	Normal	1515
6	32.6	Normal	1140
172	31.4	Normal	1230
Average			1505

CASE 4. C. B. Patient was admitted to the Roosevelt Hospital, March 28, 1934. She was a married colored woman of 37 with one child 12 years of age, and one miscarriage 11 years before admission.

A supravaginal hysterectomy was performed for a large fibroid uterus and a right salpingo-oophorectomy for "fibrous and cystic degeneration of the ovary." Pathological sections showed a normal endometrium consistent with the twelfth day of the cycle and an adenomyosis of the inner layers of uterine musculature.

The postoperative course was normal but, on the ninth day, the patient reported that both breasts

TABLE IX B.—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 7 WOMEN WITH PAINFUL NODULAR BREASTS

Experiment number	Menstruation	Pelvic pathology	Mouse units
57	30.4	Palpable cystic ovary	1740
23	26.2½	Parametrial tenderness	1550
103	29.1	Parametrial tenderness	1750
155	Amenorrhea	Posthysterectomy. Both ovaries present	760
8	27.3	Complete retroversion	1920
10	23.4	Normal pelvis	600
41	25.4	Recent oophorectomy for pseudomucinous cyst	2930
Average			1335

were secreting milk in copious amounts. This continued for 8 weeks at which time the secretion was noted as diminishing and much thinner. A month later the patient returned complaining of pain in the left shoulder and neck. Examination showed a complete cessation of secretion from the breasts, a normal vagina without evidence of atrophy and a slightly enlarged left ovary.

Hormone tests: On the sixteenth day after operation a 24 hour specimen contained 108 mouse units. Nine specimens examined during the next 6 weeks showed 24 hour excretions of 0 to 28 units. Seven specimens examined during this period for prolan by the alcohol and tungstic acid methods showed no increase over the normal.

d. The connection between menstrual abnormalities and breast symptoms was emphasized by the fact that in 82 patients the onset of the breast and menstrual symptoms was practically simultaneous. The menstrual change was a decrease in duration or frequency in 62 of these cases (Table XI).

4. Ovarian pathology in cases of chronic mastitis (Table VIII). From 21 cases observed at operation by the writer and from reports of the pelvic pathology of 47 further cases operated upon by other surgeons, one can find evidence of a relatively high incidence of cystic disease of the ovary.

For many years a condition sometimes termed pseudopregnancy and characterized by delayed menstruation with as a rule breast changes has been recognized. The symptoms are usually attributed to a persistent or cystic corpus luteum (Halban, Reeb), although Zondek (60) has shown that a persistent follicle may produce the same results. On account of an increase of folliculin in the urine and in the cyst of the ovary of his patient, Zondek (60) proposed the name polyhormonal amenorrhea for these cases. In another case with colostrum in the breasts and lutein cell cysts in the ovaries Kaiser found the Aschheim-Zondek test to be positive. Case 5 apparently belongs to this group:

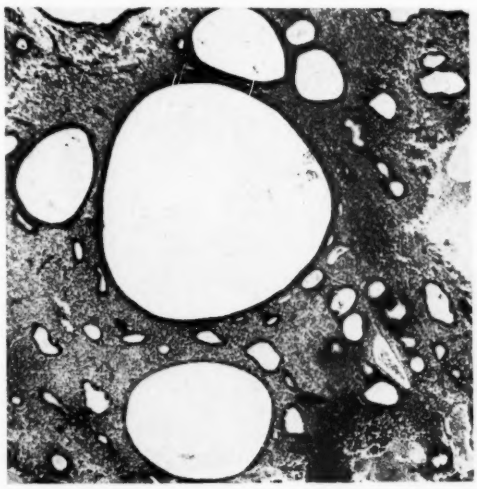


Fig. 2. SD9573. Endometrial hyperplasia in a woman of 42 with normal breasts.

CASE 5. H. G. Patient was admitted to the Roosevelt Hospital, June 19, 1933. She was a mar-

TABLE IX C.—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 6 WOMEN WITH PAINFUL BREAST HYPERTROPHY

Experiment number	Menstruation	Pelvic pathology	Mouse units
3	36.2	Salpingo-oophorectomy for cyst and inflammation	2095
44	30.1½	Partial oophorectomy for cysts	2300
66. Repeat 44	28.2	Partial oophorectomy for cysts	2835
134	28.1	Salpingo-oophorectomy for cysts and inflammation	740
34	22.8	Possible endometrial hyperplasia	3900
111	31.5	Operation for salpingitis; parametrial tenderness	1955
14	30.7	Parametrial tenderness	1765
Average			2170

TABLE IX D.—TOTAL ESTRIN EXCRETION IN THE CYCLE OF 7 WOMEN WITH ABNORMAL SECRETION FROM THE NIPPLE

Experiment number	Menstruation	Pelvic pathology	Mouse units
162	41.4	Partial oophorectomy for cystic corpus luteum	1710
118	35.8	Normal pelvis	890
166	43.5	Cervical erosion	1740
4	Amenorrhea	Posthysterectomy—one ovary removed for cysts	1500
90	33.5	Parametrial tenderness	1500
86	26.3	Complete retroversion, partial prolapse	1540
59	24.4	Complete retroversion	Traces
Average*			1480

*Average does not include case number 59

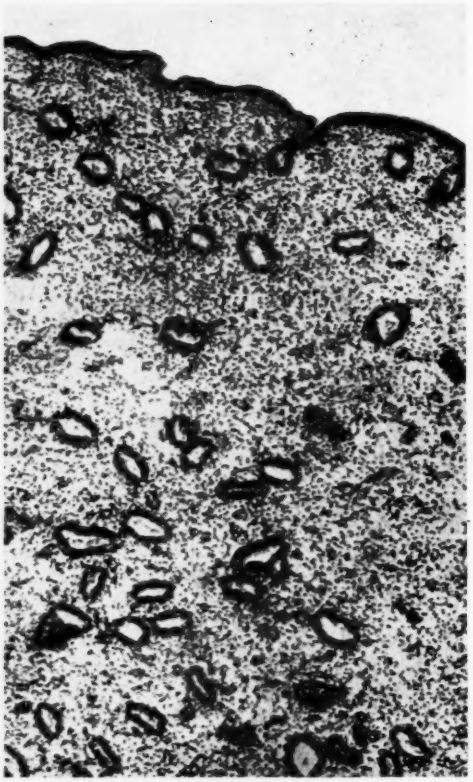


Fig. 3. SC6586. Edema of the endometrium on the fifteenth day of the cycle in a patient with retroversion of the uterus and pain and swelling of the breasts.

ried woman of 24 with 1 child 8 years of age. Menstruation had formerly been of the type, 28,4, average, with slight discomfort, but for 6 months the periods had been recurring at 5 to 7 week intervals and lasting but 1 day. For 2 years the patient had been under treatment for pelvic inflammatory disease and during this time there had been a bilateral milky secretion from the nipples and premenstrual pain and swelling of the breasts. She began to menstruate on the day of the operation after a 53 day interval.

The pathology found at operation was as follows: chronic salpingitis with adenomyosis of the uterine cornua; endometriosis and papillomas of the ovary; follicle and corpus luteum cysts of the ovary. (Fig. 1). The right ovary measured 4 by 4 by 4 centimeters and contained multiple cysts with small fibrous papillomas. The left ovary was small and adherent and measured 1 by 1.5 by 0.5 centimeters. A cyst in the right ovary, containing 8.0 cubic centimeters of clear fluid, had a hormone content of only 2.6 mouse units.

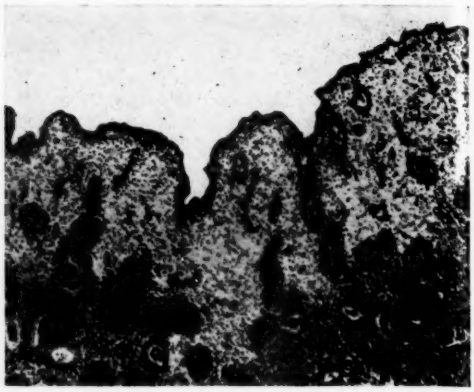


Fig. 4. SC7059. Edema and hyperemia of the endometrium on the twenty-first day of the cycle in a case with partial prolapse of the uterus and premenstrual breast pain.

The nipple secretion, irregularity of menstruation, and pelvic discomfort were only partly relieved by the operation in spite of the removal of both tubes and the right ovary. Eight months after the operation, the left ovary previously noted as atrophic had enlarged to nearly 2 inches in diameter.

The ovary with multiple small cysts was, however, a much commoner finding than the larger cysts of the type just described, particularly in cases with breast pain and diminishing menstruation. This ovarian condition, often termed "cystic degeneration," cannot at present be accepted as either the result or the cause of any known endocrine disorder. The cyst lining is usually composed of small inactive appearing cells and the hormone content of the cyst fluid is apparently low. The cystic ovary itself is often small and fibrotic and might as a rule be well under normal size were it not for the bulk of the cysts. The association of the cystic ovary with inflammation (Witherspoon) or congestion (Moench) was evident in a number of the present cases.

Four cases in which cystic ovaries had been reported at operation were studied and no hormone abnormalities noted (Table IX C). In 1 of these patients a palpable cystic ovary was present during the period of the tests, the curve of her estrin excretion being shown in Graph 4 and the history of her case being given below.

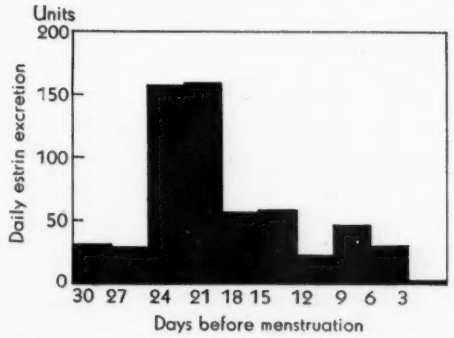
CASE 6. A. J. First examination January 13, 1932. Patient was a married woman of 29, with 1 child 6 years of age. Menstruation had always been of the 28 day type, formerly of 7 but now of 4 days duration and decreasing somewhat in amount, without dysmenorrhea. The breast symptoms dated from a pelvic operation performed 3 years before admission, when the right tube and ovary and part of the left ovary were removed for multiple follicle cysts. Since that time there had been a regular 2 day bilateral premenstrual pain in the breasts with a diffuse soreness over the entire surface of the anterior chest. In addition there had been pain in the left leg, pain in the left abdomen, a mass in the left pelvis, dyspareunia, nervousness, frigidity, and epigastric distress.

Examination showed the breasts small, dependent and slightly nodular. The fundus was of normal size and in midposition, and the cervix eroded with endocervicitis. In the region of the left ovary was a mass 5 inches in diameter, readily palpable above the symphysis. The patient remained under observation for 2½ years with examination of the pelvis every 4 months. The size of the cyst rapidly diminished after the first examination until only 1½ inches in diameter, but enlarged again to nearly its former size in June, 1933. After that, several fluctuations in size occurred. The local pelvic symptoms and the indigestion were worse when the cyst was the largest, but no correlation between the severity of the breast symptoms and the size of the cyst was evident.

The hormone tests for estrin and prolan in the blood and urine performed during a month of severe breast symptoms but with the cyst relatively small disclosed no significant abnormalities.

In 5 cases the fluid of the ovarian cysts was assayed for its estrin content. In 1 there was no hormone and in 3 only small quantities. The fifth case with profuse nipple secretion was found to have a cystic corpus luteum which yielded 20 mouse units from its 8 cubic centimeters of fluid content. In contrast with these 5, the follicle cyst in a patient with a typical case of endometrial hyperplasia (Fig. 2) without breast changes yielded 90 mouse units.

5. The endometrium in cases of chronic mastitis. In 31 cases, sections of endometrium were available for study. The 23 sections from cases with pain were normal except for 3, 2 of which showed a suggestion of glandular hyperplasia and 1 a carcinoma of the corpus. The 2 sections of endometrium from cases with hypertrophy of the breast and the 6 from cases with secretion were all normal. In the 20 cases in which the phase of the cycle at which the curettage was performed was on



Graph 4. Total estrin excretion in the 30 day cycle of a patient with painful breasts and cystic ovary. Exp. 57. Total units 1,741.

record, the endometrium showed the expected morphology.

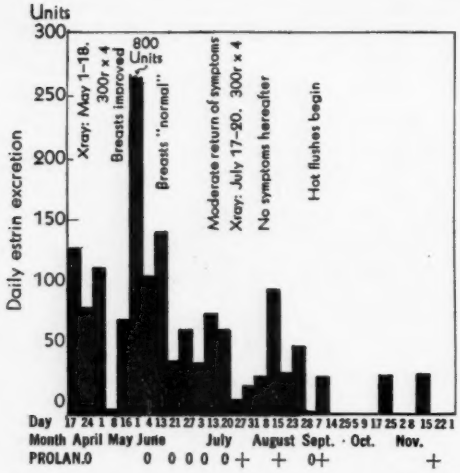
These results are important for, if chronic mastitis were due to a persistent hyperactivity of the ovary, one would expect a more or less constant association of the breast disease with endometrial hyperplasia. Actually, the clinical aspects, particularly the age of the patients and the menstrual patterns, are quite dissimilar. Only in elderly women with granulosa cell tumors have breast effects been reported in association with endometrial hyperplasia (Habbe, Muellerheim).

6. Tests for the follicle hormone. It has been noted that Frank (15) found that the normal monthly excretion of estrin in the urine varied from 800 to 1,500 mouse units, and Siebke (51) from 200 to 2,000. The five determinations made on normal women in this study showed a wider range, namely, 760 to 3,150 units.

The total monthly excretion of estrin was studied in 7 cases with pain and nodularity of the breasts, having various types of menstrual cycle and various pelvic lesions (Table IX B). The monthly rates varied from 600 to 2,930 mouse units, the average being 1,335.

The excretion of estrin was similarly studied over a month's period in 6 cases of breast hypertrophy (Table IX C). The monthly rates varied from 740 to 3,900 mouse units, the average being 2,230.

The monthly excretion in 6 cases with secretion from the nipple varied from 890 to 1,740 mouse units, the average being 1,480.


Units
300
250
200
150
100
50
0
Daily estrin excretion
Xray: May 1–18. 300r x 4
Breasts improved
800 Units
Breasts "normal"
Moderate return of symptoms
Xray: July 17–20. 300r x 4
No symptoms hereafter
Hot flushes begin
Day 17 24 1 8 16 1 4 13 21 27 3 13 20 27 31 8 15 23 28 7 14 25 5 9 17 25 2 8 15 22 1
Month April May June July August Sept. Oct. Nov.
PROLAN.0 0 0 0 0 + + 0+ +

Graph 5. Estimations of 24 hour estrin excretion at weekly intervals following radiation of the ovaries. Exp. 47. 24 hour specimens.

(Table IX D). In the seventh case studied during a course of deep X-ray therapy to the breast, there was an almost complete absence of hormone.

On account of the greater length of the menstrual cycles in the secretion group, a perhaps better contrast is obtained by noting the average daily excretion. This, for normal women, had been found to be 56 mouse units. For the three different types of breast disease the average daily output was as follows: hypertrophy, 76 units; painful nodularity, 50 units; secretion, 42 units. Although these averages are based on the assay of 232 specimens, it cannot be maintained that the differences are significant.

The estrin of the blood was studied by weekly tests by the technique of Frank and Goldberger (17) in 19 cases. The presence of the hormone was demonstrable at least once in 1 of 4 cases with pain, 7 of 9 cases with hypertrophy, and 3 of 5 cases with secretion.

7. Tests for the presence of prolan. The prolan in the urine was studied by the examination of a total of 171 specimens from 14 cases, 4 with pain, 4 with hypertrophy, and 6 with secretion. Variable methods of extraction and high degrees of concentration, in some cases to show as little as 5 to 20 units per liter, failed to give positive vaginal reactions. Minor changes in the ovarian follicles were noted when the higher concentrations were used, but these were decidedly less marked and less frequent than those commonly obtained from women in the menopause. Only in 3 cases with nipple secretion associated with delayed menses were there slight indications of an increase in prolan excretion.

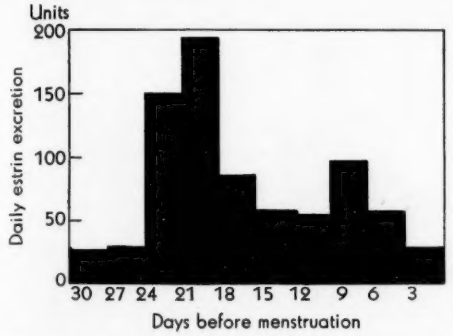
The presence of prolan in the blood serum was sought by weekly tests, using the Fluhmann (11) technique in 14 cases, 6 with pain, 4 with hypertrophy, and 3 with secretion. Some evidence of follicular ripening was apparently attained from several cases but in none was prolan definitely shown through the production of vaginal signs of estrus.

8. The effects of radiation of the ovaries. In 12 cases the effect of pelvic X-ray, and in 3 of radium from the uterus upon the clinical state of the breast was studied. In all but 1 there was immediate evidence of improvement in the pain and swelling and the nodularity of the breast tissue. In 6 cases in which the radiation dosage was sufficient completely to suppress the ovarian function, the improvement was permanent, whereas in 8 in which smaller doses were given there was a later partial return of symptoms.

In 2 cases in which X-ray of the pelvis was given, the hormone excretion was studied for 3 months after treatment by weekly examination of specimens. In both, the improvement in the breast symptoms corresponded with a decided drop in the rate of estrin excretion and by the appearance of prolan in the urine.

The effect of X-ray on the ovaries is illustrated in the following case.

CASE 7. R. L., was admitted to the hospital November 8, 1932. She was a married woman of 42 with 3 children, the youngest aged 7 years. Tenderness and diffuse nodularity of the breasts and a little oily secretion from one nipple had developed 6 months before admission or 1½ years after a supravaginal hysterectomy for fibroids. Following four treatments, each of 300 r units, to the pelvis, there was a marked improvement in breast symptoms. Two and a half months after the first series a second with the same dosage was given on account of a moderate return of the breast discomfort. Following the second series, the breast symptoms subsided entirely, prolan appeared in the urine and only traces of estrin were excreted (Graph 5).



Graph 6. Total estrin excretion in the 30 day cycle of a patient with bilateral painful hypertrophy of the breasts and a menstrual flow of 1½ days. Exp. 44. Total units 2,300.

In 2 cases an entire month's excretion of hormones was studied both before and after radiation of the pelvis. The improvement in breast symptoms was again correlated with a great decrease in estrin excretion. The history of 1 of these cases is as follows:

CASE 8. R. K., was admitted to the hospital October 1, 1931. She was 33 years of age, married but sterile. Menstruation had formerly been of the type, 28,4, average, with occasional dysmenorrhea, until 4 years ago, when she was operated upon for a uterine fibroid and cystic ovary. Following the operation the periods became reduced to 1½ days, while the breasts enlarged and developed a severe premenstrual tenderness.

During the month from April 4, to May 3, 1933, the patient's urine was collected and found to contain a total of 2,300 mice units of estrin (Graph 6). The blood tests for estrin (Frank and Goldberger) yielded positive reactions in the first and third week. No prolan was demonstrable in 10 urine specimens by the alcohol precipitation method or in 4 specimens of serum.

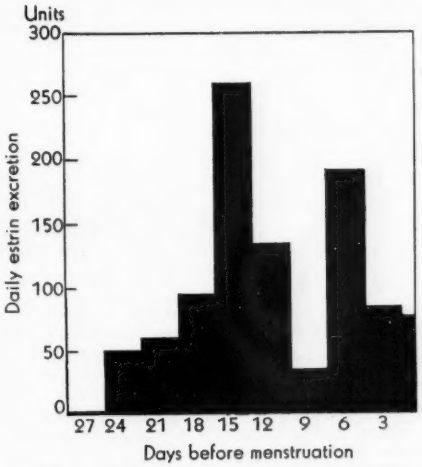
From June 5 to 8, the patient received 4 X-ray treatments to the pelvis of 200 r units each.

From June 6 to July 3, the patient excreted 2,830 mice units and had her usual menstrual period preceded by slightly reduced breast discomfort (Graph 7).

Thereafter all breast symptoms rapidly subsided and no further period occurred for 11 months.

From August 29 to September 28, the estrin excretion was studied for a third time. Only traces of estrin were discovered, the total amounting to perhaps 50 units for the month. With the return of menstruation on June 27, 1934 there was a slight recurrence of the breast tenderness.

The effect of radiation of the ovaries on the secretion of milk was less definite. In 2 cases,



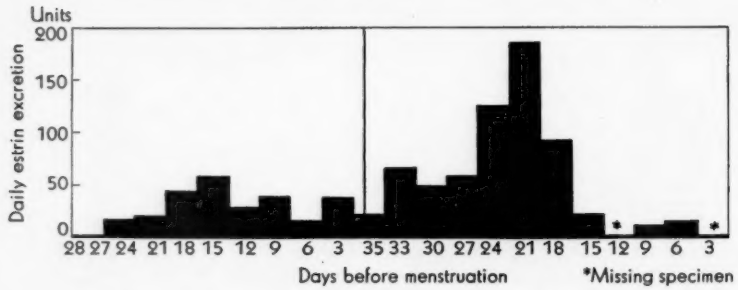
Graph 7. Total estrin excretion during the 28 day cycle following X-ray of the ovaries. Exp. 66. Total units 2,830.

the disappearance of the discharge required 3 to 4 months and in one instance milk continued to appear for 5 years after a single high voltage treatment to the pelvis in an amount to produce erythema of the skin.

Roentgenographs of the sella turcica in 3 cases of abnormal milk secretion failed to demonstrate any pituitary hypertrophy, and radiation of the pituitary by high voltage X-ray in one case failed to affect the symptoms.

9. The effect of treatment with ovarian hormones.) Improvement in the painful breast following the use of ovarian extracts has been claimed (Cutler, Leriche, Whitehouse). The fact that these results have been observed even after the administration of tablets of the dried gland, containing what now must be regarded as negligible quantities of hormone, indicates that the improvement noted was not due to the specific therapy. (Treatment of either the painful or the secreting breast at the Memorial Hospital by the injections of potent preparations of the ovary or anterior pituitary has not produced constant effects.)

In the oophorectomized woman the administration of the ovarian hormones has led to swelling of the previously atrophied breast and to some painful sensations (Werner and Collier, Loeser). On the other hand, the ad-



Graph 8. Total estrin excretion of two cycles, showing increased output during administration of hormone in a patient with bilateral painful hypertrophy of the breast. Exp. 134. Total units: first cycle, 740; second cycle, 2,185.

ministration to menstruating women with chronic mastitis of even very large quantities of hormone, sufficient to produce a demonstrable rise in the rate of estrin excretion, has not caused in our experience any increase in the breast symptoms. The following case is illustrative:

CASE 9. A. P. Patient was admitted to the Roosevelt Hospital, February 10, 1934. She was a woman of 25 with a history of encephalitis lethargica at the age of 13 and of one miscarriage 8 years before admission. A year after the miscarriage, a pelvic operation had been performed for salpingitis and a cystic ovary. Menstruation until the miscarriage had been of the type, 28,3, average, without pelvic or breast pain, but since then the periods had become totally irregular, very scant, and preceded by 2 weeks of pain, swelling and the development of lumps in the breasts. The breasts had grown progressively larger and before the periods developed petechial hemorrhages in the skin above and within the areolæ.

The patient was admitted to the gynecological ward of the Roosevelt Hospital on February 10, 1934. She was observed for 12 days before her period during which time her suffering was intense enough to require the regular administration of codeine. The hemorrhagic spots appeared 5 days before her period and are shown in Figure 12 of Part I.

During the 28 day cycle beginning February 22, 1934, no treatment was given beyond rest in bed, support of the breasts, and sedatives. Biopsies were taken on March 8, and March 22, 14 days before and 2 hours after the onset of menstruation, respectively. (Figs. 13, 14, of Part I.) There was definite improvement in the breast symptoms during this month which could only be attributed to the physical and mental rest afforded by the stay in the hospital.

Hormone tests: The excretion of estrin during this month totaled 740 mouse units (Graph 8). There were four negative blood reactions (Frank and Goldberger), the last coinciding with a weakly positive Fluhmann test for serum estrin. There was no evidence of an increase in prolan in five specimens of blood serum or in ten urine specimens extracted by the tungstic acid method.

The patient's next cycle lasted 34 days, only 14 of which she spent in the hospital. During this time she received a total of 132,000 mouse units of a commercial preparation of estrin in oil. The subsequent period was associated with a greatly reduced pelvic and breast discomfort and there were no hemorrhagic spots. The urinary excretion of estrin rose to over 2,185 units, the patient failing to submit two of her specimens (Graph 8).

10. Evidence of an associated pelvic congestion or parametritis. Reasons have been given in the first sections of the paper why a lesion of the pelvis having an effect upon the breast by way of the nervous system must be given consideration. Much of the data already discussed, including the variations in the menstrual flow and the fibrotic or multicystic ovary, might be interpreted either as evidence for a glandular or neurovascular disturbance. The conditions to be discussed under the present head (Table X) have all been described by one or more previous writers as the causes of pelvic congestion or parametritis and each has also been previously reported in association with breast symptoms. The evaluation of their importance is concededly difficult since the conditions are such that instances of each would be found in the examination of any large series of women. Certain special characteristics of these conditions as they occur in the present series, their high incidence and the frequent simultaneous appearance and disappearance of breast and

pelvic symptoms, are points in favor of a more than accidental association.

a. An existent or previous history of pelvic inflammation was noted in a total of 27 cases. These represented 12.5 per cent, 3.2 per cent, and 6.4 per cent of the cases with pain, hypertrophy, and secretion, respectively. A striking feature of these cases was that many appeared not to have been of gonorrheal origin but to have followed an abortion. The following case is illustrative:

CASE 10. G. S., was admitted to the hospital August 29, 1933. She was a married woman of 23, by occupation a night club hostess. Five years before admission she had suffered a severe pelvic infection following an abortion. For a year after that she was treated for pelvic inflammation and then operated upon. Both tubes, which were adherent and acutely inflamed, were removed.

During the last 5 years the patient's periods had been preceded by 10 days of marked pain and swelling of the breasts. Menstruation was, however, irregular occurring every 2 to 4 weeks and lasting from 3 to 7 days. Additional symptoms were diffuse premenstrual pelvic pain, abdominal distention, indigestion, leucorrhea, and dyspareunia. Examination showed the breasts of medium size, dependent, nodular in the outer quadrants and exceptionally tender. The uterine fundus was forward and fixed with attempted motion causing severe pain. The ovaries were a little swollen and very tender. The cervix was moderately eroded and discharging profusely.

Hormone tests showed a 31 day excretion of 1,955 units of estrin with four negative blood specimens. There was no evidence of an increase in prolan in 4 specimens of serum tested by the Fluhmann method or in 10 urines extracted by the tungstic acid method.

The patient was treated for a year in the gynecological clinic, at the end of which time both breasts and pelvic symptoms were greatly improved.

b. Cases of typical "chronic parametritis." Besides these cases there were 62 others with various types of pelvic pain and uterosacral or broad ligament tenderness which appeared to correspond closely to the condition, described by Freund, as parametritis and with which he noted painful nodules in the breasts. These represented 26.2 per cent of the group with breast pain, 16.1 per cent with hypertrophy, and 17.0 per cent with secretion. The following case is a good example:

CASE 11. R. S. First examination was made September 26, 1933. Patient was 30 years of age, married for 12 months, but unable to conceive. Menstruation before marriage had been of the type, 28,4, average, with moderate pelvic discomfort and a slight premenstrual swelling of the breasts. Since marriage menstruation had been every 4 weeks lasting 4 days, with very severe lower abdominal discomfort. In addition the patient suffered from constant backache, lower abdominal pain, discomfort on sitting down, dysuria, and dyspareunia to the extent of making coitus practically impossible. During this same period of 12 months the premenstrual breast pain and swelling had greatly increased and there had been a permanent enlargement of the breasts to the extent of increasing the circumference of the chest, as measured by necessary changes in the brassière, 3 inches.

Examination: The breasts were medium in size, pendulous, with a moderate amount of nodular, glandular tissue in the outer quadrants. The uterine fundus was normal in size and position but an extraordinary degree of tenderness was elicited on its attempted motion. The cervix was without erosion but secreting great quantities of clear mucus. The thyroid was a trifle enlarged.

The patient was observed at intervals for a year. The pelvic symptoms for which she primarily sought relief were always worse for several days after sexual intercourse and during 1 month that she spent by herself in the country she was largely free from both breast and pelvic complaints. In spite of numerous relapses, the tendency was toward improvement and at the time of writing she is nearly symptom free and 3 months' pregnant.

The clinical course and the subsequent pregnancy indicate that this in spite of the severity of the symptoms was a process quite distinct from the usual infectious salpingitis. An example of a perhaps later stage of the disease with decreasing menstruation has already been described in Case 2.

c. Retroversion of second or third degree or partial prolapse of the uterus was noted in 91 cases. These represented 36.6 per cent, 10.0 per cent, and 44.6 per cent of the cases with pain, hypertrophy and secretion, respectively.

TABLE X.—PELVIC LESIONS FOUND IN PATIENTS WITH BREAST DISEASE

	Cases with pain Per cent	Cases with hypertrophy Per cent	Cases with secretion Per cent
Pelvic inflammation	12.5	3.2	6.4
Parametritis	26.2	16.1	17.0
Retroversion	36.6	10.0	44.0
Endocervicitis	45.2	22.6	48.9

The relation of uterine malposition to breast disease may appear remote. Nevertheless there are three articles in the literature reporting the cure or improvement of mammary pain by the reposition of a misplaced uterus (Ayler, Hastrup, Miller). It is known furthermore that a uterus in retroversion or partial prolapse may affect the pelvic circulation to the extent of producing broad ligament varices and possibly many secondary changes. In the present series, there were 14 cases with retroversion and breast disease in which the pelvis was observed by the writer at the time of celiotomy. The uterus in these cases was regularly found swollen and congested. Histological evidence suggesting a vascular disorder in the pelvis is found in a few cases with exceptional edema and hyperemia of the endometrium and ovary (Figs. 3, 4). That this general pelvic hyperemia may affect both the ovaries and the autonomic nerves of the pelvis must be admitted.

d. Endocervicitis, erosion or infected laceration were noted in 114 cases, representing 45.2 per cent, 22.6 per cent, and 48.9 per cent of the 3 groups of cases. These are minimum figures for among those counted as normal are 27 cases not examined and 56 cases incomplete to the extent of their being no record of the condition of the cervix.

The group with cervical disease has been placed in the pelvic congestion group for two reasons. First, a hypersecretion of the cervical glands is probably often the result of pelvic hyperemia and may be its only symptom. On the other hand parametrial infection may arise through the lymphatics from a diseased cervix. In the literature are also to be found numerous reports of hypertrophied and infected cervices in association with breast disease and the cure of the latter after treatment or amputation of the cervix (Aitken, Ronth, Copland, Miller).

e. A relationship between certain breast conditions and disorders of the sexual function has been described repeatedly in the literature (Rosenthal, Glass, Samuel, Witthauer, Rufz, Dickinson). No complete statistical survey of this aspect could be made in this series, but a few points are noteworthy. In 22 patients the symptoms developed at the time of marriage. Twenty-three women complained of dyspareunia. Of 76 women questioned the majority were practicing contraception by methods which were possible causes of pelvic congestion. The relationship between a sexual difficulty and the development of physical changes in the breast is well illustrated in the following case:

CASE 12. N. D. Patient was admitted to hospital October 7, 1931. She was 28 years of age, married for 1 year without pregnancies. Six months after marriage the patient had first noted premenstrual pain, swelling, and the appearance of lumps in the breasts. Examination showed the breasts medium in size and dependent with an extraordinary diffusely swollen appearance, dilated veins on the surface, and large, partly circumscribed areas of induration in both outer quadrants. The pelvis was normal except for a hypersecretion of the cervix.

At the patient's second visit she volunteered a long story of psychological difficulties in childhood, resulting she believed in a complete inability to adapt herself to normal marital relations. Temporary separation from her husband was under consideration. Two months later the patient reported by letter that she had adopted this course and that her breast trouble had completely disappeared.

f. The time of appearance of breast symptoms. In 92 cases the onset of breast symptoms was traceable to a definite incident in the patient's life which furnished a reasonable cause for the development of a pelvic congestion or parametritis. Thus the symptoms began at marriage in 25, after abortion in 12, after childbirth in 22, following pelvic operation in 26, and coincident with pelvic inflammation in 7. In 34 cases a pelvic condition of this type was suggested by the beginning of a secondary dysmenorrhea at or near the time of onset of the breast symptoms (Table XI).

11. Dysmenorrhea and breast symptoms. Primary dysmenorrhea was present in 52 per cent of the 50 unmarried women of the series, representing 55.5 per cent of the 36 cases with pain, 60 per cent of the 10 cases with hypertrophy but none of the 4 cases with secretion. This symptom occurring with breast pain is subject to various interpretations, for on the one hand dysmenorrhea has been attributed to an increased contractility of the uterine musculature from follicular hormone stimulation (Kraus, Reynolds, Novak) and on the other it has been successfully treated by sec-

tion of the presacral nerve (Cotte, Counseller and Craig).

12. The association of thyroid disorder with breast disease. The coincidence of thyroid disorder and various types of pelvic disorder is well known. There may be, as is the case with the breast, a premenstrual thyroid enlargement as well as an apparent relationship to various menstrual anomalies, certain pelvic lesions and possibly sexual activity. In the present series there were noted 21 cases with definite thyroid enlargement and minor degrees of fullness were quite common, especially among the younger women. In 5 cases, 4 with pain and 1 with hypertrophy of the breasts, the thyroid abnormality was the only criterion for the classification of the case. The treatment of 2 cases by irradiation of the thyroid was followed by subjective improvement in the breast condition.

13. Psychic factor in breast disease. Repeated reference has been made in the literature to the excitable temperament of patients with the painful breast and the development of symptoms at times of nervous stress Taylor). Corroboration of this was found in many instances in the present series in which symptoms were made worse during periods of anxiety resulting from economic worries, the illness of relatives or marital difficulties. Pelvic symptoms from similar causes have been reported (Meyer-Ruegg). The following case illustrates the rapidity with which the breast, presumably through its vascular system, may in predisposed individuals respond to trivial psychic stimuli.

CASE 13. D. T., was admitted to hospital March 15, 1933. She was unmarried, aged 18. Menstruation, which had begun at 13, was slightly irregular, of the 21–28 day type, lasting 6 days and associated with backache, headache, abdominal pain, and cramps so severe as to cause confinement to bed.

The breasts began to develop at the age of 12 and have continued to grow. For 10 days each month there was a premenstrual swelling with severe pain radiating down each arm. In addition the patient reported that throughout the month she frequently experienced abrupt swelling of the breasts with any excitement such as a trivial accident at the dinner table, an unexpected visitor, or an anticipated social event.

Examination showed a slender white girl with enormous pendulous breasts, out of all proportion to her age and size. The breast tissue was diffusely nodular throughout, the nipples normal, the areolæ wide and dark. Rectal examination revealed a small, anteflexed uterus. The thyroid was slightly and symmetrically enlarged. The urine estrin excretion was normal but the blood test gave a positive reaction in the specimens of both the first and third week.

TABLE XI.—INCIDENTS ASSOCIATED WITH THE ONSET OF BREAST SYMPTOMS

	Cases with pain	Cases with hypertrophy	Cases with secretion	Total
Marriage	17	7	1	25
Abortion	10	0	2	12
Childbirth	16	0	6	22
Pelvic inflammation	6	1	0	7
Gynecological operation	13	7	6	26
Menstrual change	50	13	19	82
Onset of dysmenorrhea	26	3	5	34

DISCUSSION AND CONCLUSIONS

The general conclusion of this study is that a certain minimum activity of the ovary is necessary for the development of chronic mastitis but that no specific hyperfunction or hypofunction of the ovary is at present demonstrable. This result is contrary to hopes entertained at the beginning of the work and contrary to what might have been expected from the known proliferative effects of the ovarian hormone on the breast tissue.

Certain exceptions and reservations must be made. In one small group of cases in which swelling of the breast, sometimes with secretion, develops in the presence of a persistent follicle or corpus luteum cyst, a hormone cause is probable, but the clinical aspects of this condition are different from that of the common type of chronic mastitis with painful outer quadrant induration. It is not unlikely that other unrecognized reactions of the breast to certain hormone states may exist.

Even for the common type of mastitis, however, it must be conceded that the present method of study has not exhausted the possibilities of a hormone cause. Present technical methods for the clinical determinations of estrin and prolan are far from perfect and no satisfactory test exists for the quantitative

study of the corpus luteum hormone in body fluids. A very slight disturbance of gland function might cause hyperplasia in the breast when active over a considerable number of years and yet not be obvious when studied by relatively crude laboratory methods over a month's time. Irregularities in the peaks of production or excretion of estrin may furthermore have a significance quite aside from the total quantities chiefly discussed in this paper. Finally, it is possible that the abnormal estrin effects on the breasts may be the result of local conditions such as an increased responsiveness to normal quantities of hormone, possibly as the result of local hyperemia, or a tissue concentration of the gland substances, bearing no relation either to the actual activity of the ovary or to the amount of hormone in the blood stream.

With these reservations, the following summary is offered of the present knowledge of the conditions under which chronic mastitis is found to develop.

A. THE PAINFUL NODULAR BREAST

1. An active ovary producing estrin must be present.

a. The painful breast is limited to women before the menopause and after puberty.

b. The pain and nodularity improve with X-ray and surgical castration, such improvement paralleling the fall in estrin excretion in the urine.

2. There is no indication of an extensive ovarian activity.

a. The histological structure of the painful breast does not show the uniform epithelial proliferation of a hormone produced hyperplasia.

b. The 7 cases studied did not contain any excess of estrin in the urine or blood and in several cases the estrin excretion was quite low.

c. The endometrium in cases of the painful breast does not show the hyperplasia to be expected with hyperactivity of the ovarian follicle.

d. Administration of considerable quantities of ovarian hormone to patients with the painful breast does not increase the severity of the symptoms.

3. There is no indication of an underfunction of the ovary.

a. The average excretion of estrin in 7 cases which were studied was within normal limits and in several of these cases rather high values were found.

b. The scant menstruation noted in 16.9 per cent of the women with the painful breast was the chief evidence for the underfunction theory, but the estimation of the estrin excretion in such cases gave normal values.

c. Consistent results have not been obtained in this clinic by the treatment of the painful breast with estrin or the ovary stimulating hormone of the anterior pituitary.

4. A "dysfunction" of the ovary remains a possibility which cannot be entirely excluded.

a. Delayed or irregular menstruation, which must be accepted as a sign of a disturbed ovarian function, was present in 13.7 per cent of the cases.

b. Irregularities in the curves of estrin excretion or of blood concentration may eventually be shown to have some significance, but knowledge for their interpretation is at present lacking.

c. The multicystic ovaries observed in so many cases also may be taken as evidence of a disturbed ovarian function but they may be looked upon as well as the result of vascular congestion in the pelvis.

5. A corpus luteum disorder cannot be excluded since tests do not exist for studying the blood and urinary levels of this hormone.

a. The frequency of normal menstrual rhythm, the histological evidence of a regular endometrial cycle, and the rarity of evident disease of the corpus luteum in patients operated upon are evidence against this factor.

6. There is no indication of a hyperactivity of the anterior pituitary.

a. Prolan appears in the urine only in cases of pronounced underfunction of the ovary, which is never found with the painful breast.

b. An increase in prolan in the urine comparable with that taking place in the menopause has been excluded by the present series of studies.

c. The appearance of prolan in the urine after X-ray of the ovaries occurs at the time of improvement of breast symptoms.

7. The painful breast has from the clinical viewpoint a large nervous element.

a. The pain and tenderness are more marked than are to be expected in an endocrine produced glandular hypertrophy.

b. The pain radiates to the arm, neck, axilla and lateral body wall and may be associated with hyperesthesia of the skin of the whole thorax.

c. The pain and swelling in certain cases are produced or become worse during periods of nervous tension and may even develop abruptly within a few minutes after a nervous shock at any time in the monthly cycle.

d. Various associated nervous complaints are described by the patient including insomnia, anxiety, palpitation, blurring of the vision, mucous colitis, and headaches.

e. One case report exists in the literature of the disappearance of the premenstrual breast symptoms in one breast after the destruction of the thoracic sympathetic of that side.

8. A local state of vascular congestion is a prominent feature of the painful breast.

a. The gross appearance of the painful breast before menstruation with its hyperemia of the areola, venous dilatation, and increased weight alone suggests hyperemia.

b. The histological signs of this vascularity may be demonstrated in the "edema" of the lobule.

c. The relief afforded by the onset of menstruation is usually too rapid to be explained as the result of epithelial regression.

d. The sudden appearance of pain and swelling in the middle of the cycle in certain cases cannot be ascribed to epithelial proliferation.

e. Simple support of the breast often causes considerable amelioration of symptoms.

f. In one case described with pain and hypertrophy, petechial hemorrhages occurred regularly before menstruation in the skin about the areola.

9. The coincident gynecological lesions and menstrual disturbances have a possible significance as evidence of an associated vascular congestion and tissue edema in the pelvis.

a. The common pelvic lesions are classifiable as adnexal inflammation, parametritis, retroversion, and cervical infection.

b. The onset of pelvic symptoms and breast pain after marriage, abortion, or pelvic infections is significant of parametrial congestion or inflammation.

c. The scant menstruation may be regarded as the effect of the secondary fibrosis in the pelvis described by many writers as the end-result of chronic pelvic congestion.

d. The edematous, cystic, and fibrotic ovaries may have a similar cause.

One may offer the following provisional conclusions on the cause and nature of the painful, diffusely nodular type of mastitis as follows:

1. The ovarian hormone is certainly a necessary factor, but it has not been possible by present laboratory methods to demonstrate any specific abnormality of ovarian or anterior pituitary function. It is, however, possible that refinements in technical methods may eventually reveal a definite endocrine disturbance.

2. The conception of the disease as primarily a vascular disturbance with changes occurring in the interstitial tissues of the breast based on abnormal nervous stimuli explains many of the clinical aspects of the disease. Such a view can only be accepted with caution, however, because it requires the assumption of a physiologic mechanism yet largely undemonstrated.

B. BREAST HYPERTROPHY OCCURS IN AT LEAST TWO FORMS

1. In one group in which there is a simple painless enlargement of the breasts of relatively uniform consistence an endocrine factor is clearly prominent. This includes the hypertrophy developing in childhood and in old women in the presence of the specific ovarian neoplasms, such as the granulosa cell tumors and teratomas. Breast swelling has also been observed in the presence of persistent corpus luteum and follicle cysts and ascribed to a polyhormonal amenorrhea. Breast hypertrophy after hysterectomy may, in some cases, have a similar basis.

2. The painful hypertrophies of this study were not of this type and resembled closely the tender nodular breasts, both in regard to their physical characteristics and the condi-

tions under which they occurred. Hormone studies of a series of these cases gave normal blood estrin values, rates of monthly excretion of estrin a little higher than in the cases of the painful breast, but still probably within normal limits, and no increase in prolan excretion. X-ray of the ovaries led to a disappearance of the pain and to a reduction in the size of the breasts but the use of ovarian hormone by mouth or hypodermic was ineffectual. The coincident pelvic lesions and the incidents associated with the onset of the breast enlargement were in general the same as those found for the painful breast.

The conclusions in regard to the causes of this type of hypertrophy must be similar to those for the painful, nodular breast.

C. ABNORMAL SECRETION FROM THE NIPPLE

The local physical characteristics as well as the conditions under which abnormal nipple secretion occurs seems to distinguish it somewhat from the two preceding groups: the average age of these patients was higher; the proportion of women with preceding pregnancies was much greater; menstrual disturbances were more frequent, particularly in the form of delayed menstruation; the average daily excretion of estrin was lower; the secretion did not disappear at once after X-ray of the ovaries.

In many cases, however, the characteristics of the painful breast were present, notably the cyclical pain and swelling, the diffuse nodularity and certain coincident pelvic lesions.

It is concluded that the cases with abnormal secretion are a heterogeneous group, the following representing a possible classification of these.

1. Cases with a non-specific discharge, serous, sanguineous or purulent, from local disease of the larger ducts.

2. Cases reported in the literature with a definite nervous factor either in the form of direct stimulation of the nipple, or a central nervous system disease, such as tabes dorsalis or syringomyelia.

3. Cases reported in the literature with definite evidence of endocrine disease, such as the instances of amenorrhea with follicle or corpus luteum cysts. To this group may belong the cases of temporary secretion in the early menopause, theoretically ascribable to the sudden decrease in ovarian activity or the increased function of the anterior pituitary.

4. In a large group of cases one is forced to maintain the alternative theories noted for the other two types of breast disease, namely an as yet undetermined variety of endocrine disturbance or a little known form of neurovascular disorder.

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REPRODUCTIVE EFFICIENCY BEFORE AND AFTER THE BIRTH OF MALFORMED CHILDREN

A Study of 405 Consecutive Families

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THIS is the second report dealing with families in which malformed children have been born. The first one concerned the place-in-family of the defective child (2).

The present communication deals with the remaining pregnancies in these families. It concerns, primarily, those which did not terminate normally, and which may be classified as "disturbed," a "disturbed" pregnancy being defined as one which ended in either a miscarriage (including abortions), a stillbirth or a premature birth. The chief interest of the study concerns the closeness of the disturbance to the defective child.

If miscarriages, stillbirths, or premature births should take place closer to the defective child pregnancy than would be expected according to the laws of chance, it would suggest that both these disturbed pregnancies and the defective child pregnancy were but different expressions of a prolonged period of decreased reproductive power. If this were so, it would seem to lend weight to the hypothesis that congenital malformations are due to defects in the germ plasm taking place before the moment of fertilization. Whereas, if the disturbed pregnancies occur at random in the family, there would be less reason to believe that the reproductive power of the mother exhibited any prolonged period of weakness. The present report attempts to elucidate this theoretical conception.

Materials and methods. To quote from the first communication: "There were found in the files of the Bureau of Vital Statistics, Department of Health of the State of Pennsylvania, 130,132 death certificates for stillborn and liveborn individuals who died in Philadelphia during the 5 year period between January 1, 1929, and December 31, 1933. Each of these certificates was examined, and the data on those noting the existence of any congenital defect, were transcribed to duplicate, official forms. Fourteen hundred and seventy-six such certificates were located.

"The deceased individual was considered to have possessed a defect under either of two conditions: (1) if the defect involved the surface of the body, or (2) if internal, its presence had been disclosed by operation or necropsy. Diagnoses not conforming to these requirements were considered as not verified and were excluded from further consideration. This procedure reduced the number of usable certificates to 890, or only 60 per cent of the original 1,476 certificates.

"An attempt was made to interview the mother of each of the 890 deceased individuals, the visits being made in the summer of 1934 by 3 fourth year medical students. A complete reproductive history was secured from each mother that could be located. The group forms a consecutive series. All of the defective children died within a given geographical area and within a given period of time."

In order to have a homogeneous group of reproductive records for analysis, it was necessary to omit from consideration certain families forming the group of 539 families reported upon in the first paper. Families in the above group, having the following characteristics, were not used in the present analysis: (a) Those with more than one defective child; (b) those families in which there was only a single conception; (c) families in which the mother was married twice and in which families the defective child was born to the second husband. This procedure reduced the number of families from 539 to 405.

RESULTS

Diagnosis of defective child. In the 405 families, there were 405 congenitally malformed children (Table I, column 2). The most frequently recurring chief diagnoses (column 1)

TABLE I.—DIAGNOSIS OF CONGENITALLY MALFORMED CHILD

Diagnosis	Children					
	Total		Disturbed pregnancies		Undisturbed pregnancies	
	Number	Per cent	Number	Per cent	Number	Per cent
(1)	(2)	(3)	(4)	(5)	(6)	(7)
Reported	405	100.0	151	100.0	254	100.0
Hydrocephalus	86	21.2	29	19.2	57	22.4
Spina bifida	73	18.0	26	17.2	47	18.5
Anencephalus	48	11.9	17	11.3	31	12.2
Hydrocephalus, spina bifida	31	7.6	7	4.6	24	9.5
Pyloric stenosis	29	7.2	12	7.9	17	6.7
Heart disease	25	6.2	10	6.6	15	5.9
Monster	16	4.0	7	4.6	9	3.5
Intestinal obstruction	10	2.4	5	3.3	5	2.0
Craniorachischisis	9	2.2	3	2.0	6	2.4
Hare lip, cleft palate	8	2.0	3	2.0	5	2.0
Gastroschisis	6	1.5	3	2.0	3	1.2
Microcephalus	6	1.5	3	2.0	3	1.2
Meningocele	6	1.5	1	.7	5	2.0
Others	52	12.8	25	16.6	27	10.5

Showing in column 1, the chief diagnoses that occurred most frequently in the families which form the basis of the present report; in column 2, the frequency with which the various defects were observed; in columns 4 and 6, the relative frequency of the defects as they appeared in families *with* and *without* any disturbed pregnancies. Note that there was no essential difference in the frequency with which the different defects were observed in the two groups.

and the number of children in each group (column 2) are recorded in this table. Hydrocephalus was the most common defect; spina bifida, with and without hydrocephalus, and anencephalus were the next most frequent diagnoses.

In the 405 families, 151 families, or 37.3 per cent, had one or more disturbed pregnancies (Table I, column 4) and 254, or 62.7 per cent, had no disturbed pregnancies (Table I, column 6). These two groups can be compared in Table I with respect to the diagnoses of the malformed children in each. There appears to be no essential difference in regard to the types of defects found in the two groups.

In the 405 families, there were 1,732 conceptions (Table II). Over 60 per cent terminated normally, with live born, fully developed offspring. Twenty-three per cent resulted in the birth of malformed infants, and 13 per cent resulted in either miscarriage, stillbirth, or premature birth.

The relative positions of the various disturbances of pregnancy, in relation to the position of the conception which resulted in the birth of the congenitally malformed child, are shown in Table III. The position of the defective child pregnancy is indicated by the heavy face, horizontal line. The place-in-family of all other conceptions is shown in column 1. In this column, the place immediately preceding that which ended in the birth of the defective child is indicated by -1; the conception which followed immediately that of the defective child is indicated by $+1$. The conception preceding, and next but one to the defective child conception, is indicated by -2, and the conception following, next but one to the defective child pregnancy, is indicated by $+2$, and so on. The observed frequencies of miscarriages, stillbirths, and premature births by birth position, in relation to the position of the defective child are indicated separately in columns 2, 3, and 4. Their observed, combined frequencies are given in column 5. Their expected, combined frequencies, had they been distributed by birth position according to the laws of chance, are shown in column 6.

The latter distribution was computed by the use of the Greenwood-Yule reconstruction (1). The method is as follows: The expectancy that a characteristic occurring at random will take place in any particular position depends upon the size of the family. For example, in a family of three siblings, in which there is one defective sibling, there is one-half a chance that each of the two remaining siblings will be affected; in a family of four siblings, in which one sibling is malformed, only one-third a chance exists that any one of the three remaining siblings will be affected.

Using this method, the fractions contributed to each birth position by each family were totaled by birth position for the entire group of families. In those in which there were two disturbed pregnancies, each position was allotted double the fractional value given to families with only one disturbed pregnancy. In families with three disturbed pregnancies, each birth position was given triple the birth value given to those families with only one disturbed pregnancy, and so on, depending on the number of disturbed pregnancies in the family.

Since all disturbed pregnancies in each family were counted in the total of column 5, and since in column 6, each family was counted once for each disturbance noted in column 5, the total of these two columns are necessarily approximately equal.

The ratio of the observed, combined frequencies of the disturbed pregnancies (column 5) to their expected, combined frequencies (column 6) is shown in column 7. Had the observed disturbances occurred with random frequency in the various birth positions, the figures in each birth position in column 5 would have been, for all practical purposes, identical with those in column 6. This identity would have produced a ratio in column 7 of 1.0 for each birth position.

The figures in column 7 show that the disturbed pregnancies in the position -1 and $+1$, immediately adjacent to the defective child, occurred more often than would be expected according to the laws of chance. In the birth position immediately preceding that of the defective child, the observed disturbances were the most frequent, being next most common in the position immediately following that of the defective child. In the majority of the more distant positions, the disturbances occurred less often than would be expected by chance. Three of the distant positions (-3, -6, -9) showed a greater frequency than would be expected by chance. These values are believed to be false due to the fact that the number of families forming the total group was so small.

TABLE II.—MALFORMED OFFSPRING AND DISTURBED PREGNANCIES IN 405 FAMILIES

Conceptions	Conceptions	
	Number	Per cent
Total	1732	100.0
Terminating normally	1094	63.2
Ending with malformed offspring	405	23.4
Ending with miscarriage, stillbirth, or premature birth	233	13.4

Showing the number of conceptions experienced by 405 mothers, each having one malformed child, and the number of disturbed pregnancies among the remaining pregnancies. Note that more than one-third of all of the pregnancies were abnormal.

Considering the relative sizes of the observed frequencies in the -1 and -2 positions, column 5, it is evident that the frequency in the -1 position is approximately two and a half times that of the -2 position. These figures refer to the combined miscarriages, stillbirths, and premature births. If these combined disturbances of pregnancy are sub-grouped, as shown in columns 2, 3, and 4, the following is observed: The frequency of miscarriages alone (column 2) in the -1 position is more than twice as great as in the -2 position; the frequency of stillbirths (column 3) in the -1 position is two and a half times as great as in the -2 position; and the frequency of premature births (column 4) in the -1 position is over three times as large as in the -2 position. These individual observations lead one to conclude that the nearness of the miscarriages, the stillbirths, and the premature births to the position of the defective child were individually determined by a common cause, and by the same cause, which, in all probability, brought about the congenital malformations in the families in this group.

TABLE III.—THE OBSERVED AND EXPECTED DISTURBANCES OF PREGNANCY

Conception place-in-family	Observed				Expected	Ratio Col. 5 ÷ Col. 6
	Miscarriages	Stillbirths	Premature births	Combined miscarriages, stillbirths, premature births	Combined miscarriages, stillbirths, premature births	
	Number	Number	Number	Number	Number	
(1)	(2)	(3)	(4)	(5)	(6)	(7)
−12	1	0	0	1	.63	—
−11	1	1	0	2	.63	—
−10	1	1	0	2	2.33	.86
− 9	2	1	1	4	2.75	1.45
− 8	1	0	1	2	4.94	.41
− 7	2	1	0	3	7.14	.42
− 6	6	4	1	11	9.63	1.14
− 5	9	0	2	11	12.58	.88
− 4	5	3	2	10	17.98	.56
− 3	15	8	6	29	25.41	1.14
− 2	19	6	4	29	35.75	.81
− 1	45	15	14	74	56.60	1.30
+ 1	29	6	5	40	37.66	1.06
+ 2	8	3	1	12	13.79	.87
+ 3	3	0	0	3	3.65	.82
+ 4	0	0	0	0	0.71	.00
+ 5	0	0	0	0	0.17	.00
+ 6	0	0	0	0	0.17	.00
Totals	147	49	37	233	232.52	—

The heavy face, horizontal line indicates the place-in-family of the congenitally malformed child. The minus numbers in column 1 represent the conceptions which preceded the defective child; plus numbers, those which followed. The −1 position represents the conception immediately preceding, and +1 the one immediately following the defective child. The figures in columns 2, 3, and 4 represent the observed miscarriages, stillbirths and premature births, and in column 5 they are combined. The expected frequency of the combined miscarriages, stillbirths, and premature births in column 5, had they occurred at random, is shown in column 6. The ratio of the observed to the expected figures is shown in column 7.

On the basis that 1.0 is normal expectancy, the figures in column 7 show that the disturbances of pregnancy (column 5) occurred more often than expected in the positions close to the defective child, and less often in the more distant positions. The small number of families studied accounts for the ratios greater than 1.0 found in the −3, −6, and −9 positions.

RECAPITULATION

The above observations suggest that mothers who give birth to congenitally malformed individuals exhibit varying length periods of decreased reproductive efficiency. In most cases, this period covers only the time required for the conception and birth of a single child. In other instances, the period is longer, and during this time, in addition to the conception and birth of the malformed child, other conceptions take place which also do not end normally.

Since these disturbances of other pregnancies tend to cluster about the pregnancy which results in the birth of the congenitally malformed child, and because all of the disturbances and the malformations vary in character and degree, one from the other, their multiplicity lends weight to the hypothesis that congenital malformations are due to defects in the germ plasm, rather than to forces which may operate upon the fertilized egg.

The finding of the disturbance so often in the pregnancy immediately preceding that which results in the deformed child, suggests that the appearance of a disturbed pregnancy should make the obstetrician suspect the pos-

sible existence of a congenital malformation during the course of the succeeding pregnancy.

SUMMARY AND CONCLUSIONS

1. The reproductive activity of 405 mothers, each having had a congenitally malformed child, is reported with respect to the incidence of miscarriages, stillbirths, and premature births.

2. Of the 405 families, 151, or 37.3 per cent, exhibited one or more miscarriages, stillbirths, or premature births.

3. Of the total of 1,732 conceptions in the 405 families, 63.2 per cent ended normally, 23.4 per cent resulted in malformed children, and 13.4 per cent ended in either miscarriage, stillbirth, or premature birth.

4. Miscarriages, stillbirths, and premature births occurred more often than would be expected by chance in the pregnancies immediately preceding and immediately following the pregnancy which resulted in the birth of the defective child, and less often than would be expected by chance in the remaining pregnancies. Miscarriage, stillbirth, and premature birth occurred most often in the pregnancy immediately preceding that of the defective child.

5. From the above observations, it is concluded that the birth of a congenitally malformed child may be only one expression of a prolonged decrease in functional reproductive activity, the other expressions being miscarriages, stillbirths, and premature births.

6. It is suggested that the obstetrician has unusual reason to suspect the possible existence of a congenital malformation in the pregnancy which follows immediately after a miscarriage, a stillbirth, or a premature birth.

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LOCAL ANESTHETICS PRODUCING PROLONGED ANALGESIA: ELIMINATION OF PAIN AFTER RECTAL OPERATIONS

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THE most important unsolved problem in proctology today, with the exception of a cure for cancer, is the elimination of pain after rectal operations. This holds true because, if we cannot operate on patients without causing severe postoperative pain, we cannot operate on most of them at all. Most patients wish to avoid a rectal operation anyway, and if there be also the knowledge that operation will be followed by hours of extreme suffering, they will drag around with trouble for years rather than come for relief. Their apprehensions are not without basis. After the usual ligature operation for hemorrhoids, the routine orders of Miles are given: ½ grain of morphine shortly after operation, then tincture of opium every 4 hours for 24 hours, then every 6 hours for 24 hours, and then every 8 hours for the third and fourth days. An article just published on postoperative care by Best states that after all is done to relieve postoperative pain, the patient is likely to need morphine and codeine. Patients who have received such doses of narcotics say that they feel dizzy, but still suffer.

Rectal surgery becomes thoroughly satisfactory to all, when, after an operation under local nerve block, the patient can sit up in bed, enjoy a good rest, is free from pain, comfortable, and perfectly happy. That this can be approximated in the majority of patients will be shown.

Elimination of pain after rectal operations demands both an open type of operative technique, and also the use of anesthetic solutions having a prolonged local analgesic action for 3 days after operation. The factor of operative technique will be touched upon briefly later; the main portion of this study is devoted to a new understanding of local anesthetics of prolonged action.

Of such anesthetics, some have been recommended so recently that their properties have not been understood. Some are dangerously toxic. Some are likely to cause undue tissue irritation or sloughing. Heretofore, we have been left largely to guess work or to experiments on patients, without accurate laboratory measurements to know beforehand just what concentration of these solutions would or would not cause tissue injury. The purpose of this paper is to present measurements of the local irritation and of the duration of local anesthesia produced by various agents.

THE SOLUTIONS STUDIED

Quinine and urea dihydrochloride. A practitioner in the rural districts of Arkansas (Thibault), in using quinine by hypodermic to treat malaria, discovered its prolonged local anesthetic properties, and popularized its use in the double salt of quinine and urea dihydrochloride.[1] This salt makes a strongly acid solution and although the official name has been quinine urea hydrochloride, the more accurate name is quinine urea dihydrochloride.

This preparation was abandoned by the general surgeons, who found that it caused induration, edema, and sometimes sloughing; but it is still used by a number of excellent proctologists in rectal surgery where its irritant properties are less deleterious.[2] Arthur Crookall of Portland, Oregon, has used it in ½ per cent solution in 1,000 cases and states that in these it never caused a slough. He does not claim that in this weak concentration it entirely eliminated postoperative pain, but he does claim that it lessens the pain. Finsterer used this same ½ per cent concentration in

[1] Quinine had been previously suggested as a local anesthetic by Griswold.

[2] Hertzler found by histological section of areas injected with quinine and urea that this induration is due to the deposit of fibrin interstitially, and not to cellular infiltration. Quinine prevents cellular infiltration (27).

The prolonged anesthetic action of quinine is due to the fact that it can prevent its own absorption from its local deposit. After the injection of a solution in the muscle of a dog, Mariani found that 17 hours later two-thirds of the dose could be recovered and quantitatively measured by excising the injected area (37). The mechanism of the action of quinine by preventing its own absorption and removal from the local injection side may be explained as follows: It raises the surface tension of the body fluids, which forces the leucocytes to round out in globular balls. They cannot extend their pseudopodia for phagocytic action because the high surface tension on their outer surfaces forces them to stay in smooth spheres without any projecting pseudopodia. Probably also there is an anti-enzymatic action on the tissue fluids preventing its removal (68).

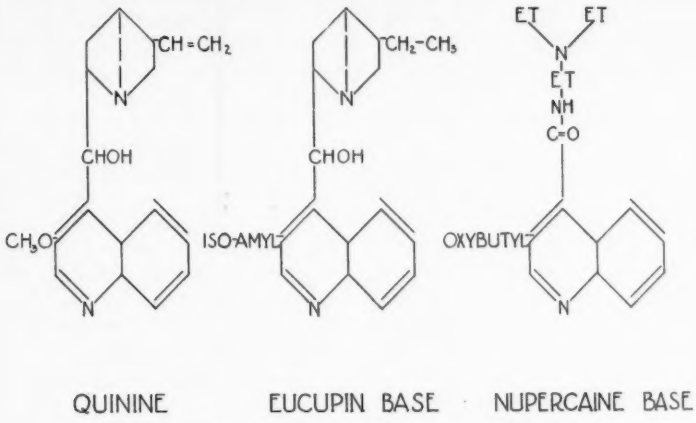

Fig. 1. Eucupin, modification of quinine molecule.

rectal surgery. Saphir (56), of New York City, has used it in ½ to ¼ per cent solution in over 2,000 hemorrhoidectomies, and at first reported that in these low concentrations, there were no sloughs. More recently he has had sloughing even in the 0.5 per cent solution in water and has abandoned it (57). In stronger concentrations, usually 5 per cent, it has been used for injection under anal fissure by W. O. Green, A. B. Graham, Yeomans, Hirschman, E. G. Martin, and others.[1] I shall show that it causes unnecessary pain on injection and unnecessary danger of sloughing, and that better solutions are available.

Quinine hydrochloride with urethane. So far as I know I am the first person to use this solution for local anesthesia. While working with it in experiments on a different problem, I discovered by accident that not only was it less painful, but also less irritating and less likely to cause a slough than quinine urea dihydrochloride.[2]

Eucupin. By modifying and lengthening two side chains of the quinine molecule, the anesthetic potency to the rabbit's cornea may be raised 3,000 per cent: eucupin (isoamylhydrocupreine) is one of these modifications (Fig. 1). It was first synthesized as a bactericidal substance and found to be bactericidal to streptococcus in 1: 4000 and to staphylococcus in 1: 800 (45) (bacteriostatic to staphylococcus in 1: 160,000). While using it in the eye, Morgenroth discovered its high potency as a local anesthetic. Its prolonged action is explained by the fact that it remains in the tissues locally and may be recovered for analysis 4 days after it is injected (3).

Henius, in Germany, has used it in a 2 to 5 per cent ointment or suppository for relieving the pain of anal fissure. It has also been applied in ⅓ to 2 per cent aqueous solution to ulcerating carcinoma both for its anesthetic action and also to clean up secondary infection.

Vuzin (iso-octylhydrocupreine) belongs to the same hydrocupreine series as eucupin but has a longer side chain. Lipschitz and Freund (34) found that it inhibited cell oxidation only half as much as eucupin and this suggested the likelihood that it might cause less local irritation than eucupin. The hemolysis tests of Bijlsma and of Schmidt also suggested that it might be less irritating than eucupin. Fromherz found that it effected a more prolonged anesthesia of the sciatic nerve of the frog than eucupin. It was therefore included in the studies to follow.

Nupercaine is something like a hybrid of quinine and procaine containing as it does the

[1] Martin now uses the quinine urea hydrochloride under anal fissure in 3 per cent after experiencing sloughing with the 5 per cent (57).

[2] This solution was first injected subcutaneously in the treatment of malaria. Pain was found to be less after its injection than after the injection of other quinine solutions (16). Later, because of its solubility, it was introduced by Genevrier in a highly concentrated solution for the injection treatment of varicose veins. The supersaturated solution in water used for varicose veins must not be used for anesthesia.

TABLE I.—MINIMAL LETHAL DOSES PER KILOGRAM BODY WEIGHT IN THE RABBIT AND COMPARATIVE AMOUNTS OF CLINICAL SOLUTIONS WHICH WOULD THEREFORE BE EXPECTED TO BE LETHAL TO A 70 KILOGRAM MAN

Effective clinical concentrations of solutions	M.L.D.* grams per kilogram	Subcutaneously—Amount solution expected lethal to 70 kilogram man—c.cm.	M.L.D.* grams per kilogram	Intravenously—Amount solutions expected lethal to 70 kilogram man—c.cm.
Procaine HCl ½%	.350 (37)	4,900	.030 (38)	630
Tutocaine HCl ¼%	.200 (39)	11,200	.015 (39)	840
Nupercaine 1/10%	.005 (34)†	350	.002 (40)	140
Quinine HCl 1% with urethane ½%			.046 (41)	326
Diothane ¼%	.300 (42)	840	.015 (42)	420
Vuzin di HCl			.015 (43)	
Eucupin base 1/10%	More than .150 (a)‡	10,500	.0125 (18)	840

*M.L.D., minimal lethal dose.
†The findings of Lipschitz and Laubender as to subcutaneous M.L.D. was checked and confirmed by the author of this paper.
‡See text.

quinoline ring of quinine and the diethylaminoethanol radical found in many of the procaine series (a-butyloxycinchonic acid diethylaminoethylene diamide hydrochloride). It was synthesized by Karl Miescher and studied by Uhlmann, Lipschitz and Laubender (35), and others. Though it has been often described, it is so little understood that its abuse, rarely its legitimate use, has resulted in frequent deaths. To this point we shall return later. The fact that in spite of these accidents its use is apparently increasing proves the urgent need for local anesthetics with a prolonged action.

Diothane has 2 substituted phenyl urethane radicals contained in a total molecule which is otherwise suggestive of the procaine series. It has been synthesized by Rider and suggested for prolonged local anesthesia (50, 51).

Benacol is a solution of equal parts of paramino benzoyl benzoate and phenmethylol in 90 parts of rectified sweet almond oil. It has been used extensively by Yeomans and his associates in the treatment of intractable pruritis ani. In England, it is used at St. Mark's Hospital by Gabriel for pruritis ani, and anal fissure. H. T. Hayes, in Houston, has used it also at the close of hemorrhoidectomies, injecting small amounts under the operative wound to give prolonged local anesthesia.

Anucaine is a new preparation in oil resembling benacol, but having in addition one part of butylamino benzoate and ⅛ part of novocain base.

Procaine hydrochloride concentrated in a solution of 5 per cent has been mentioned by Schmidt as giving a longer anesthesia than nupercaine 1: 1000 when both are used with adrenalin. As such a strong solution of procaine is less toxic than the weak solution of nupercaine, it was included in the determination which follows.[1]

Tutocaine hydrochloride is a member of the procaine series which is about twice as potent as procaine hydrochloride and only half as toxic on subcutaneous administration to animals. Instead of the ordinary ¼ to ½ per cent solution, it was tried for prolonged anesthesia in a concentrated solution of 2½ per cent.

Before comparing the local irritation caused by these solutions, it is well to have in mind their general toxicity.

COMPARATIVE TOXICITY

The comparative toxicity of these solutions must be considered from the standpoint of exact measurements in animals and then also from clinical experience.

Animal experimentation. Measurements of toxicity in animals are shown in Table I. In this table, there is included for comparison the well known anesthetics of short duration, procaine and tutocaine. The first column lists the solutions in concentrations effective for anesthesia. The second column shows the amount of clinically effective solutions which would be lethal subcutaneously to a 70 kilogram man if he were equally sensitive to the solutions as the rabbit. In the fourth column is shown the minimal lethal dose intravenously in the rabbit. In the fifth column is

[1] Pantocaine, a member of the procaine series with an anesthetic potency ranking with nupercaine and only half as toxic, was not included in these studies because it was shown by Wiedhopf, by Ernst, and by others that in wheals made by strong solutions, the duration of its anesthesia (23 to 25 minutes without adrenalin) is not much longer than procaine hydrochloride 1 per cent. When applied topically, it has a more prolonged action, but its toxicity precludes its topical application in large quantities of concentrated solution in large rectal wounds.

TABLE II.—PROTECTION BY NEUTRALITY (ACID BASE), ISOTONICITY, AND URETHANE AGAINST LOCAL IRRITATION BY QUININE SALTS—0.15 CUBIC CENTIMETER INTRADERMAL WHEALS IN RABBITS' FLANKS

	Results*	Per cent sloughs
1-a. Quinine HCl ⅓% in quinine urea diHCl ½% in water	oeoeoooeo	
1-b. Quinine HCl ½% in quinine urea diHCl 0.7% in water	oSoooooo	
2-a. Quinine HCl 0.7% in quinine urea diHCl 1% in water	SoeoooeoSo	
2-b. Quinine HCl 0.7% in quinine urea diHCl 1% in .425% saline	oooooooo	
3. Quinine HCl 1% in .425% saline	SSSSSSoS	88
4. Quinine HCl 1% with urea 0.17% in quinine urea diHCl 1.4%	eSSSeSoSoo ooSSeSoSSoSoSoSo	46
5. Quinine HCl 1% with urea 0.5% nearly neutral in .425% to 0.85% saline	Sooeoeeo SoeoSeoooe	17
6. Quinine HCl 1% with urethane 0.5% fresh mixture (nearly neutral) in .425% to 0.85% saline	oSeooooooo oooSoooe	12
7. Quinine HCl 1% with urethane 0.25% fresh mixture—adrenalin 1:1000 .5 c.cm. in 0.85% saline 100 c.cm.	SeeSoeo	
8. Quinine HCl 1% with urethane 0.5% old mixture (nearly neutral) in 0.85% saline	oooooooooeeee	o
9. Quinine HCl 1% with urethane 0.5% old mixture (nearly neutral) in 0.85% saline, with adrenalin	oeooeeeeoo oooooo	o

*S, Sloughs; e, Erythema; o, No sloughs

shown the amount of clinically effective solution given intravenously which would be lethal to a 70 kilogram man if he were equally sensitive to the solution as the rabbit.

No previous record of the minimal lethal dose of eucupin administered sucutaneously to the rabbit has been located in the literature. Accordingly, 0.150 per kilogram body weight of eucupin base or 0.170 per kilogram body weight of eucupin dihydrochloride was injected subcutaneously into 8 rabbits and they were kept alive for 14 days. None of these died or showed the slightest toxic symptoms. Two rabbits were given 0.300 kilogram per body weight of eucupin base subcutaneously. One lived and one died within half an hour. The minimal lethal dose to the rabbit must, therefore, be over 0.150 per kilogram body weight subcutaneously. Bijlsma gave 0.025 per kilogram body weight subcutaneously to one kitten and the kitten died on the sixth day. I have given 4 times this dose to 2 kittens without the slightest toxic symptoms for 6 days.

It will be seen from Table I that when solutions of equal anesthetic potency are injected into the rabbit, eucupin solutions may be used safely in the largest amounts and nupercaine in the smallest amounts. In these concentrations, more than twice as much eucupin solution may be injected into the rabbit subcutaneously as procaine hydrochloride and thirty times as much solution of eucupin base as nupercaine solution of equal anesthetic power. Indeed, if man were equally susceptible to eucupin as is the rabbit, and water intoxication be disregarded, the amount of clinically effective anesthetic solution required to be lethal by subcutaneous infiltration would be about 3 gallons!

Although the toxicity of solutions administered subcutaneously varies in different animals including man, the intravenous lethal dose per kilogram body weight does not have such wide variations, and, therefore, the comparison of intravenous toxicity is shown (Table III). Here again the superiority of eucupin in freedom from toxicity is shown as well as the limitations of nupercaine.

Clinical estimate. From the clinical standpoint, we find that quinine hydrochloride urethane in a highly concentrated solution has been injected into man intravenously in varicose veins several hundred thousand times with only one reported fatality from toxicity (Matas).

The possibility of peculiar individual susceptibility to eucupin has been investigated by Dawson and Garside, who found that because of the long and branched side chain in

its molecule, natural idiosyncrasy to eucupin is unlikely (8), although idiosyncrasy may be acquired (7).

Twenty-four deaths from nupercaine have been reported (see appendix). When it is used, we should be on our guard against its toxicity, using these precautions: First, large doses of barbiturates should be given before operation, as this probably gives protection against its toxicity (63, 64, 69). Second, in view of the considerable number of deaths known to be due to injection of solutions made by mistake 10 times too strong, in 1 per cent instead of 1/10 per cent, it is safer not to resort to the local pharmacist to make up the solution, but to use the large 25 cubic centimeter ampules of 1:1000 solution recently made available by the manufacturers. Third, in view of its extraordinary toxicity if injected into a vein or venous sinus, the technique of local infiltration must be perfect in order to prevent such an eventuality, especially when in hemorrhoidectomy, injection is made near a ligated blood vessel. Fourth, in view of a fatality with only 90 cubic centimeters 1:1000 solution, injection of concentrations greater than 1:1000 or in amounts greater than 50 cubic centimeters should be made with caution.

LOCAL IRRITATION

There is a need for a new method for measuring tissue irritation caused by local anesthetics, which I shall submit. Older methods have had partial values.

Anesthetic solutions for a long time have been injected into rabbits' ear lobes where the skin on the outer side of the lobe comes close to the skin on the inner side of the lobe, to see if they would cause sloughing. Experience in this method (32) has shown that it is not sufficiently delicate for a test of local anesthetics. For example, it has been found that small amounts of 2½ per cent quinine urea dihydrochloride do not make sloughs by this test, and even 5 per cent of the same solution does not always do so, but there is abundant clinical evidence to show that a 2½ per cent solution of quinine and urea dihydrochloride may cause sloughing.

Another test instills the anesthetic solution into the conjunctival sac of the rabbit to see if conjunctivitis follows. This method lacks a sharp endpoint. It measures the effect on topical application to a peculiarly developed structure rather than the effect of infiltration. It allows only 2 tests on each animal, whereas the test which is to be submitted allows 8 or more tests to be made on each animal and measures the direct effect of infiltration.

A third test measures the hemolytic action of the solution to be tested on red blood corpuscles. This test, while not new, has recently been explored thoroughly by Schmidt and has considerable value. However, it has certain handicaps. It assumes that a non-nucleated red blood corpuscle will respond to possible irritation by local anesthetics, as do the nucleated cells of the tissue. Imagine here the bizarre results which must be expected if a hemolysis test were made on such a solution as quinine urethane, inasmuch as we know that urethane acts to take quinine promptly out of serum to fix it in the red blood corpuscles (40). It does not take into account the vasoconstrictor or vasodilator effect of the solution to be tested, on the local circulation. It does not allow measurement of the effect on irritation, of such added substances as adrenalin and urethane, which we shall show to be important. In practice, it does not check with infiltration tests: For example, Bijlsma found that vuzin dihydrochloride had only half the hemolytic effect of eucupin dihydrochloride on erythrocytes suspended in Ringer's solution, and that even when serum was added the effect was about equal (3). Yet the experiments which I shall report indicate that vuzin dihydrochloride when infiltrated is more irritating than eucupin dihydrochloride. This may be explained by the fact that eucupin is a vasodilator and vuzin a vasoconstrictor[1] (Bijlsma). Hemolysis tests do not take into account such action.

The method to be submitted uses intradermal wheals made in the flanks of rabbits. If this method has not been used before it is probably because of the difficulty in removing the hair. Shaving the rabbit's hair, plucking it, or using a depilatory, must be avoided, since all such procedures cause so much irritation as to interfere with measurements of

[1]However, Odermatt found some vasoconstrictor action in eucupin.

the irritation due to the solution injected. A high speed electrical veterinarian's clippers, on the stretched skin, if aided by frequent brushing of the hair from its teeth, will remove the hair close to the skin without irritating it. Two or three such patches are made in each flank, between the ventral and dorsal areas. Care must be taken to keep away from the gluteus maximus and biceps femoris muscles, as sloughing is more likely to occur in this region. If the patches are too close to the artery located over the shoulder, sloughs which would occur elsewhere would not be observed. If the hair which remains interferes with the observations, it should be wetted. Two injections of 0.15 cubic centimeter each are made into each one of the two patches, making 8 in all. In case uniform results are not obtained, a much larger number of injections may be made.

These intradermal injections make a delicate test because the solution lies under the horny epidermal cells with poor blood supply and, therefore, a slough is more apt to occur by this method than in ordinary tissue infiltration. Comparison with the wheals that have been produced in the skin of the human thigh indicates that rabbit skin is more sensitive. The delicacy of this test can be still further increased by the addition of adrenalin to the solution.

In the protocol which follows, it will be noted just what concentrations of nupercaine, eucupin solutions, quinine urea dihydrochloride, quinine hydrochloride and urethane, diothane, and benacol and anucaine can be injected in amounts of 0.15 cubic centimeter intradermally in the rabbit with and without sloughing. These tests have been made with aqueous and isotonic solutions, with and without adrenalin. An "S" is marked where a slough occurred, an "o" where there was no change, and an "e" where there was erythema without sloughing. I made more than 1,300 of these wheals in rabbits and give reports where the findings proved of practical significance.

The optimum solution for quinine. It will be seen from Table II that the highest concentration of quinine and urea dihydrochloride in water which can be used without sloughing is ½ per cent quinine and urea (containing ⅓ per cent quinine hydrochloride). This is important because it shows that this laboratory method agrees in results with clinical experience in the thousands of cases reported by Crookall, Finsterer, and Saphir.

Quinine hydrochloride in 1 per cent solution in saline gave sloughs in nearly every wheal (88 per cent sloughs). When the same concentration of quinine hydrochloride 1 per cent was used in ordinary quinine urea dihydrochloride 1.4 per cent, less than half (46 per cent sloughs) of the wheals sloughed. This shows that the addition of urea does prevent some of the irritation of quinine, as is generally accepted. But a very much greater improvement came when (a) the amount of urea was increased to 0.5 per cent, (b) no hydrochloric acid was added, and (c) 0.425 per cent saline was used instead of water (17 per cent sloughs).

Still greater was the improvement when urethane was substituted for urea. A fresh solution of quinine urethane caused only 12 per cent sloughs. A well aged solution of quinine hydrochloride and urethane kept for 3 weeks showed no sloughs at all. Even when adrenalin was added (and we shall see later that the addition of adrenalin increases greatly the tendency of most solutions to slough), a well aged solution of quinine urethane was used in 18 wheals without a slough. One may conclude that about three times as strong a concentration of quinine hydrochloride can be used in a well aged solution with 0.5 per cent urethane, even with adrenalin added, without sloughing, as can be used when made up with urea and hydrochloric acid in water in the ordinary quinine and urea dihydrochloride. This is the first advantage of quinine urethane solution over quinine and urea dihydrochloride.

A second advantage is that quinine urethane keeps better than weak solutions of quinine and urea dihydrochloride, which tend to deteriorate because, as Giemsa found (16), the urea decomposes to form alkaline ammonium which precipitates the alkaloid quinine, and this process probably is accelerated when the quinine and urea are in a less acid solution. This may be the reason, certainly

a good one, why quinine and urea have been used in an acid solution. But when urethane is added, this trouble is avoided, for it has been known for a long time (16)—and I have confirmed this—that quinine with urethane if not saturated does not precipitate on standing.

There is a third reason for the superiority of quinine hydrochloride with urethane over quinine urea dihydrochloride; quinine and urea dihydrochloride causes an immediate violent pain at the site of injection. Quinine urethane causes little if any such pain, as any one may verify.

Fourth, intracutaneous wheals were made by injecting urea dihydrochloride and quinine hydrochloride urethane. The first showed a wide border of erythema around them; the quinine hydrochloride urethane did not. This indicates that quinine urethane is less irritating.

One may conclude that a well aged solution of quinine hydrochloride urethane with sodium chloride added to isotonicity, and adrenalin, is superior to the classic solution of quinine and urea dihydrochloride.

Protective action of urethane. It has been known to Frohlich, to Winkler, and to Danzen Peng, that the systemic administration of urethane in large doses inhibited the irritant action of mustard oil on the skin; but no previous reference has been found to the fact that infiltrated locally, small concentrations of urethane added to quinine have a protective action against irritation and sloughing.

The change which urethane makes is not that it merely prevents inflammation[1]. Inhibition of inflammation might actually lessen the resistance of the tissue to injury. But my experiments show that it actually prevents tissue injury and sloughing.

The action does not seem to be on the pain nerves for while urethane 5 per cent is anesthetic, concentrations below 2½ per cent are not (23). It does not seem to protect by action bringing in a better supply of blood and serum to the site of injection because there is less redness around a wheal into which quinine urethane is injected than when wheals are made with quinine urea dihydrochloride or nupercaine. That urethane like urea has a lytic action on the fibrin (42) laid down by quinine and thus prevents irritation, is one possibility. Another is that the protective action of urethane is exerted not on the tissues but chemically on the quinine. It has been noted that when urethane is added to quinine there is a change in the lines of the absorption spectrum (19). This has been ascribed by de Thron (10) to the formation of quinicin or quinotoxin, an isomere of quinine, which Sollmann (61) showed was, contrary to its name, not exceedingly toxic. However, the quinotoxin occurs only in 3 per cent in de Thron's findings, and one therefore questions whether this can explain the protection conferred by urethane against tissue injury. It might seem more probable that the urethane combines with the quinine[2] probably at the unsaturated double bond in the vinyl side chain. In this connection it may be noticed that nupercaine, the least irritating of the quinolin anesthetics also has a structure suggestive of a substituted urethane.

The fact that aging of the solution of quinine urethane makes it less irritating may be explained on two grounds: Either time and sunlight allow the urethane to become more thoroughly united with the quinine molecule, or else the quinine turns to quinicine (quinotoxin). This problem is now being studied.

Effect of osmotic pressure. It will be seen from a study of the controls in Table IV, that 3 wheals made with distilled water out of 18, caused small sloughs, whereas none of the 12 made with physiological saline made sloughs. This shows the importance of isotonicity even without the addition of adrenalin.

A further study of the controls shows that procaine hydrochloride and tutocaine hydrochloride can be used in aqueous solutions with adrenalin, without sloughing. This, however, does not hold at all for the other solutions.

In the case of nupercaine, although the manufacturers rightly advise its use in saline, the importance of this is not generally realized. I have found one of our ablest surgeons using

[1] Ikeda has shown in the frog that, in contrast to many other substances, urethane and ethylhydrocupreine cause only slight inhibition of leucocytic migration.

[2] Mattei has shown that urethane exerts profound changes on the pharmacological action of quinine, carrying it out of the blood serum and fixing it in the blood corpuscles for 96 hours and at the same time hastening its elimination from the kidneys.

TABLE III.—TISSUE IRRITATION BY LOCAL ANESTHETICS, 0.15 CUBIC CENTIMETER INTRACUTANEOUSLY IN RABBITS' FLANKS

Solution	In water	Approximately isotonic	In water with adrenalin	Approximately isotonic with adrenalin†
Distilled water or saline	ooooSoSSoo	oooooooooo	oSoeoooo	oooooooo
Procaine HCl 1%			oooooooo oooooooo	
Tutocaine HCl 1%			oooooooo	
Procaine HCl 5%			oooooooo	
Nupercaine 4/10%		ooooSeeee		
Nupercaine 3/10%		oooooooo		oooooSS
Nupercaine 2/10%			eSSoSSSS	oooooooo
Nupercaine 1/10%	oooooooo		SeeeeSSS	oooooooo
Eucupin base 1/10% HCl 10% .2 c.cm. in 100 c.cm. Tutocaine ½%	ooeSSSSooooo	ooooooooeeoo	oSooSSSSo	oooSeSSooooooo
Same with urethane ½%				ooooooeooSo SeSeooeS
Eucupin base 1/10% HCl and NaOH to dissolve procaine HCl 1%	SoooSoSo	oooooooooo‡		
Vuzin base 1/10% in Vuzin diHCl 11/100% 10% HCl .5 c.cm. to 100 c.cm.				SSoeoSeoSS
Eucupinotoxin in 2/10%				SSooSSSe
Diothane 1%	SSSSSSSSSo	oeeSSSoo		
Diothane ½%		oSooooooooooooee oooooooooooSSoo SSooSSeeoo		
Diothane ⅓%	ooSeSoSo			
Benacol (oily)	SSSSSSSS			
Anucaine	SSeSSSSS			
Nupercaine in oil	SSSSSSSSSSSSSSS SSSSSS			

S, Sloughs; e, Erythema; o, No sloughs*

*In some early experiments where erythema occurred without sloughing, a zero was recorded.
†Adrenalin was used 0.5 c.cm. of 1:1000 solution in 100 c.cm.
‡No procaine hydrochloride added.

nupercaine in an aqueous solution. The experiments in Table III show that nupercaine 1:1000 in water with adrenalin is likely to cause sloughing. Twice as great a concentration can be used with adrenalin in saline without sloughing.

Again, in the case of eucupin, tests show (Table III) the importance of isotonic rather than aqueous solutions, illuminating one of the mysteries of medical history. De Takats, of Northwestern University, performed over a hundred operations with eucupin in saline without a single slough. One hundred intradermal wheals which he made caused no sloughs. Then other workers (44) used it in solutions which were "water solutions in the majority of cases" and had sloughs. As a result of their condemnation, the surgical world did nothing further with eucupin. How did it happen? The protocols in Table III show that both sides were right in their experiments. Twenty-one wheals made with eucupin hydrochloride in saline caused no sloughs. Twenty wheals made with eucupin hydrochloride in distilled water did show frequent sloughs.[1]

Clinicians sometimes assume that, because sodium chloride 0.85 per cent is isotonic with

[1] I must warn against the solution tried by Picard which is made in water in 0.2 per cent and is likely to cause sloughing.

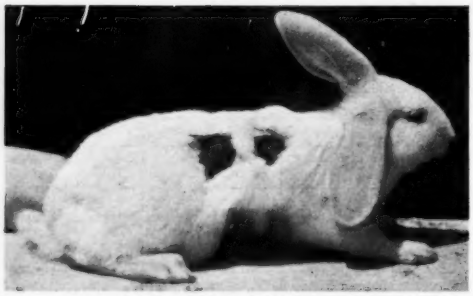

Fig. 2. Sites for intracutaneous wheals for tests of local irritation by anesthetic solutions.

body fluids, procaine hydrochloride is isotonic in the same concentrations. This is a wrong assumption. Procaine hydrochloride is not isotonic in 1 per cent but in 5.48 per cent (4). Eucupin in a 1 per cent procaine solution or a half per cent tutocaine solution is far from being isotonic.

Effect of adrenalin. The results of experiments with the addition of adrenalin shown in Table III were an unpleasant surprise. The addition of adrenalin is necessary for the prolongation of analgesia for several days. Yet these experiments show that in all these solutions tested, except procaine and tutocaine, the addition of adrenalin greatly increased the tendency to tissue injury. This was unfortunately true to a marked degree with eucupin.

Effect of acidity on eucupin. Table IV shows the desirability of keeping anesthetic solutions, such as eucupin, away from the acid side. This agrees exactly with tests on the conjunctival sac made by Sollmann (60), by Copeland (5) and by Gifford (18), showing less irritation if solutions are kept nearly neutral. However, a solution buffered in borax boric acid, made on the suggestion of Gifford's work, was not free from sloughing tendency when adrenalin was added.

Vuzin is shown by the tests to be more irritating than eucupin.

Diothane. I have no judgment to pass on diothane for topical application; but the tests made for infiltration in Table III show that in aqueous solution, the form in which it is recommended, it has a pronounced sloughing tendency. The addition of saline partly helped

TABLE IV.—EXPERIMENTS TO MODIFY TISSUE IRRITATION BY EUCUPIN 0.15 CUBIC CENTIMETER INTRACUTANEOUSLY IN RABBITS' FLANKS

All solutions approximately isotonic

Effect of pH.	Without adrenalin	Adrenalin 0.5 c.cm. in 100 c.cm. solution
Eucupin base 0.12% in Eucupin di HCl .15% pH. 4*	ooSSSoooo	
Eucupin base 0.15% 10% Phosphoric Acid 0.25% pH 5.4	oooooooo	
Eucupin base 0.1% from Eucupin di HCl .12% Boric acid 0.8% Borax qs pH 6.4		oSeeeeSoSS
Eucupin base 0.1% Emulphor e 2% pH 3.9		SSooSSSo

*Hydrogen ion concentration taken from report of Copeland and Notton.

S, Sloughs e, Erythema o, No sloughs

this but caused an early precipitation of the diothane.

Benacol had a destructive action. Sloughs were large and deep. It would seem to be painful, for even the long suffering rabbit who did not squirm upon the injection of any other solution except distilled water, jumped, and squirmed, or actually cried out in loud squeals when wheals were made with benacol. It may be desirable for the destruction of subcutaneous nerves in pruritis ani, but one feels reluctant to class it as a local anesthetic.

Anucaine was equally destructive, causing sloughs in nearly every wheal. So also did nupercaine in oil.

Although an anesthetic solution, for the purposes of rectal surgery to be described, must not cause too much irritation, it is not necessary that such a solution have the perfect freedom from irritation which is a *sine qua non* of general surgery:

First, in general surgery there must be prompt union of the tissue layers and such union must not be delayed. In rectal surgery many of us prefer to leave wounds wide open to be healed by second intention. Second, it is known that solutions which might cause sloughing if injected in an area where the tissues are under pressure will not cause sloughing if there be no pressure or tension. In closed surgery with the wound sewed up

tight, there is postoperative tissue edema and sometimes pressure. This is avoided in open types of rectal surgery. Third, in rectal surgery a cause of delayed healing is the spasm of the sphincter muscle after operation, which grips the operative wound so tight as to cause ischemia. Prolonged local anesthesia prevents this vise-like grip of the sphincter, prevents the ischemia and thus facilitates healing. Fourth, in rectal surgery in the lower area in the skin below the mucocutaneous line, delayed healing may be actually desired when fissures and infected crypts need prolonged surgical drainage.

On the other hand one has reason to protest against the common use, even in rectal surgery, of some of these irritant, if not destructive, solutions. There is especial danger of postoperative hemorrhage when such solutions are injected into the anal canal near the large branches of the inferior hemorrhoidal artery.

COMPARATIVE ANESTHETIC POWERS

Of the large number of methods previously devised to measure the anesthetic power of solutions, two are of outstanding importance. First, the intracutaneous wheal to measure the potency of anesthetics for infiltration, and second, instillation into the rabbit's conjunctival sac to determine whether or not the solution paralyzes the corneal reflex. It will be shown later that deduction from the rabbit's cornea test, if applied to oily solutions, may lead to errors, and a new test will be presented to measure the power of local anesthetics on topical application, utilizing directly the open wound.

In using tests on the intracutaneous wheal, I have sought to avoid errors made in the past. How unsatisfactory past methods have been is shown by the wide divergence in results. For example, in measuring the duration of anesthesia in the wheal made by procaine hydrochloride, pharmacologists of high standing report results in the wheal made by procaine hydrochloride varying from 9 minutes to 35 minutes, and in the wheal made by nupercaine, a duration varying from 35 to 100 minutes (28). Exactly the same amount of anesthetic must be injected into the wheal or

Fig. 3. Testing of surface anesthesia with Harvard inductorium.

wide variations in the duration of anesthesia will result. I have used 0.4 cubic centimeter because this gives a large enough wheal to avoid doubtful readings. Still more important is the choice of an instrument to test anesthesia in the wheal. The wisp of cotton, the pin prick, and the blunt wire all cause error, because the tip may contact a point in the skin between nerve endings. An associate tested the skin of my forearm with the twisted wisp of cotton and found that in 3 places of 15 so tested without any previous injections of anesthetics the wisp of cotton could not be felt. A stroke with a pin, or the use of an electric current between two terminal wires covers enough space to catch a nerve ending, which may be missed by contact at a point. The pin scratch method has the advantage of avoiding the irritation caused by the electric current. On the other hand, the electric current has the advantages of giving a clearer endpoint and of measuring pain sensation without admixture of touch and pressure sensation. In these experiments electrical stimulation was used between the ends of 2 fine wires conveyed from an inductorium.

The first column in Table V shows the duration of anesthesia when adrenalin was not added to the solutions. The solution of quinine urethane gave a much longer anesthesia than the solution of quinine urea dihydrochloride. Nupercaine gave anesthesia of shorter duration than eucupin.

The second column shows that when adrenalin was added, nupercaine gave a more prolonged anesthesia than eucupin with tutocaine and adrenalin.[1] Nupercaine with tutocaine

[1] De Takats, in wheals on the forearm, obtained anesthesia for 7 hours from the eucupin tutocaine adrenalin solution. My results show a much shorter duration; but my tests with electrical stimulation give a much stronger stimulation than the skin scratch which he used.

gave a still longer anesthesia. Quinine hydrochloride with urethane gave a partial anesthesia lasting for more than 3 days.

Procaine hydrochloride with adrenalin concentrated in 5 per cent gave longer anesthesia than nupercaine 1:1000 with adrenalin. A strong solution of 2½ per cent tutocaine gave a still longer anesthesia.

It should be emphasized that these wheal tests are only of value in giving an idea of the duration of anesthesia by one solution as compared with another. They do not give an idea of the absolute duration of analgesia. Although eucupin tutocaine adrenalin solution gives anesthesia for not over 2 hours by my tests in the wheals, clinical experience agrees with that reported by de Takats,[1] that this combination sometimes gives analgesia for about 3 days.

PROLONGED ANESTHESIA BY TOPICAL APPLICATION

Attempts to produce prolonged anesthesia by topical application to the open wound date back to 1921 when Vogel, of the University Clinic of Marburg, applied a 2 per cent solution of eucupin with adrenalin to the pharynx after tonsillectomy. Such attempts failed for several reasons: First, the addition of adrenalin to eucupin solutions invalidates them for topical application: when adrenalin is added to eucupin for infiltration, the anesthetic action is prolonged because the vasoconstrictor action of the adrenalin prevents the removal of the anesthetic away into the general circulation and causes it to exert its action locally in full force. When adrenalin is added for topical application, the opposite effect is obtained: the vasoconstriction resulting from the adrenalin prevents local absorption of the anesthetic solution, so that little, if any, of the anesthetic gets into action.[2] Previous solutions of eucupin for topical application (74) have been used in very high concentrations which were too irritating. Finally, in earlier days but little was known as to preventing the stinging effect of strong solutions of eucupin when applied to the open wound.

It is commonly assumed that the rabbit's cornea test may be used to estimate the comparative potency of anesthetics for topical application to other surfaces such as the open wound. That this common assumption may lead to egregious errors seems indicated by experiments hereinafter described. It is true that the rabbit's cornea test gives some idea of the comparative potency of aqueous solutions; but it is quite unreliable as a measure of the potency of solutions in oily bases on the open wound. Morgenroth long ago showed that oily solutions of the bases of eucupin and other hydrocupreines anesthetized the rabbit's cornea. I have tried the same experiment with nupercaine ointment on the rabbit's cornea and obtained excellent anesthesia. Probably because of such findings, we are now having it advertised for local application for prolonged anesthetic effect to all sorts of open wounds and mucous membranes, but especially to rectal wounds.

Clinically, nupercaine ointment applied in the open wound does not begin to give any such anesthesia as ought to be expected from its powerful anesthetic action on the rabbit's cornea. Accordingly, a method was devised for measuring the potency of local anesthetics topically applied to the open wound. In rabbits, under ether anesthesia, the peri-anal skin and mucous membrane were removed down to, and partly into, the sphincter muscles. After the animal had entirely recovered from the anesthetic, an electric current was applied to the wound from an inductorium strong enough to make him jump. On one side nupercaine or other ointments were then applied; on the other side eucupin solutions were applied. These were held in contact for 5 to 8 minutes. Then electrical stimulation was applied to each side and the results compared. It is necessary not to hold the tail up, as this inhibits reaction.

When this test with nupercaine ointment was made on 13 rabbits, not once was anesthesia obtained. Every time, stimulation made the rabbit jump where nupercaine ointment had been applied. On the other side in all of 7 rabbits tested, eucupin solution from ½

[1] De Takats, in wheals on the forearm, obtained anesthesia for 7 hours from the eucupin tutocaine adrenalin solution. My results show a much shorter duration; but my tests with electrical stimulation give a much stronger stimulation than the skin scratch which he used.

[2] Accords with the work of Sollmann who found that the addition of adrenalin interfered with the action of quinine urea dihydrochloride on the rabbit's cornea (59).

per cent to 9/10 per cent in water always produced partial anesthesia and usually complete anesthesia. Eucupin ½ per cent in physiological saline solution was not so effective as the eucupin in water.[1]

Nupercaine 1 per cent solution was not tested against the 1 per cent nupercaine base in ointment because strong solutions of nupercaine are too toxic to be used in large amounts.

Someone may inquire, "But does not an oily solution act better because it stays there longer slowly feeding out the anesthetic?"

This might be true of an anesthetic of short action, but we are now dealing with anesthetics which after absorption in the tissues give a prolonged action. As a matter of fact, these anesthetics are so extremely soluble in oily bases as compared with the tissues that they are not absorbed well from their nest in the oily base. Possibly the reason why they do anesthetize the cornea and not the open rectal wound may be found in the fact that the cornea has neither blood vessels nor lymphatics which would carry away the absorbed drug. Moreover, the nerve fibers in the cornea are non-medullated.

TABLE V.—COMPARATIVE DURATION OF ANESTHESIA — INTRACUTANEOUS WHEALS, 0.4 CUBIC CENTIMETER ON ABDOMEN — 3 WHEALS WITH ADRENALIN — 4 WHEALS WITHOUT ADRENALIN—TEST WITH HARVARD INDUCTORIUM

Solutions	Without adrenalin	With adrenalin*
1. Physiological saline (control)	No anesthesia.	
2. Distilled water	Less than 35 min.	
3. Quinine urea dihydrochloride in water 0.5%	1 hour 20 min.	
4. Quinine urea dihydrochloride 0.5% in saline	Less than 45 min.	
5. Quinine hydrochloride 1% Urethane ½% in physiological saline	Complete 1 hr. 30 min. Partial 5 hours	Complete 5 hours Partial 3 days
6. Nupercaine 1/10% in saline	1 hour	Between 2 and 3 hours
7. Nupercaine 1/10% in saline with tutocaine 0.5%		3 hours 15 min.
8. Eucupin base 0.1% Hydrochloric acid 0.2% Tutocaine 0.5% in saline	Complete 1 hr. 30 min. Partial 2 hours	Between 1½ and 2 hours† Partial 3 hours
9. Procaine HC 5% in water		3 hours 10 min.
10. Tutocaine HC 2½% in 0.425 saline		4 hours 10 min.
11. Eucupin base 1% in rectified sweet almond oil (one wheal only)	No anesthesia—redness and pain	

*Adrenalin 1:1000 was added 0.5 c.cm. to each 100 c.cm. of solution.
†When adrenalin 0.1 c.cm. was added instead of 0.5 c.cm., the duration of anesthesia was unchanged.

CLINICAL FINDINGS

From the laboratory findings presented, one should expect quinine urethane solution to be far superior to all other known local anesthetics of prolonged action, because, when such solutions, in the highest concentrations which can be used without sloughing, are compared, quinine urethane solution gives by far the longest anesthesia. Clinical experience, however, raised an unexpected difficulty when quinine urethane solution was used for infiltration in operative surgery: it prolongs the bleeding time so that the wound may ooze for 2 or 3 days. For this reason it was abandoned in operative surgery.

On the other hand quinine urethane has justified expectations for the purpose of injection of anal fissure. It can be used in a higher concentration without sloughing than can quinine urea dihydrochloride, it is more stable, and, most important, it does not cause such severe pain on injection as quinine urea dihydrochloride. Of course any anesthetic solution, even procaine hydrochloride, will cause pain if injected under some hypersensitive fissures, but quinine urethane solution is much less likely to cause pain than quinine urea dihydrochloride. It is now being used in a concentration of quinine hydrochloride 1 to 3 per cent, with urethane in half the concentration of the quinine. Usually 1 or 2 cubic centimeters are injected under a fissure.

Quinine urethane solution may also prove of value in the injection treatment of pruritis ani.[2]

It must be warned that the supersaturated solution of quinine urethane used for varicose

[1] Similarly Hertzler found that in aqueous solution the absorption of procaine hydrochloride by the peritoneum was more rapid than when the procaine was dissolved in physiological saline.

[2] If quinine urethane is mixed with novocain suprarenin solution "K," which is the common form sold in ampuls, a gelatinous precipitate forms. This is due to potassium sulphate added to the ampu las a stabilizing agent, which precipitates quinine. This difficulty can be avoided by using ordinary bulk procaine hydrochloride or a tablet of tutocaine.

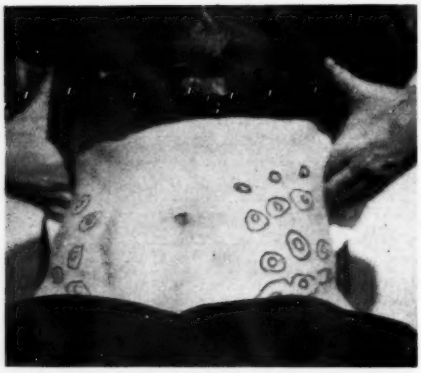

Fig. 4. Sites of wheals to determine duration of anesthesia. Note absence of areola of redness around quinine urethane wheals.

vein injection is too strong for any of these purposes.

EUCUPIN FOR TOPICAL APPLICATION

Three-fourths per cent eucupin base with just enough 10 per cent hydrochloric acid, added drop by drop to dissolve, in water, has proved to be of great value in postoperative wounds after fistulectomy, excision of pilonidal sinuses, and hemorrhoidectomy. Indeed, in large fistulectomy wounds infiltration is impracticable and topical application is the only method available. Eucupin solution, not nupercaine solution, should be used for this purpose because nupercaine solution is too toxic to be used in the high concentrations and large amounts needed for topical applications. Eucupin is also relatively inexpensive. The same patient who has had nupercaine ointment applied with little or no relief will tell you that there is no comparison between the two methods, that after the eucupin solution there is complete relief of pain sometimes for 12 hours or more.

Eucupin, 0.75 per cent solution, is also being applied topically in cases of prolapsed, strangulated, gangrenous hemorrhoids. Such cases are not usually operated on by competent proctologists in this stage. Eucupin applied both relieves pain and keeps down infections.

One of the chemists who prepared the 0.1 per cent solution of eucupin buffered in borax boric acid, heretofore described, dropped this into his nose for the relief of hay fever. Ephedrine gave him relief for only 15 minutes. This eucupin solution made his nasal passages perfectly clear for 24 hours and nearly clear for a second 24 hours.

TECHNIQUE OF EUCUPIN APPLICATION

Upon topical application of eucupin 0.75 per cent solution in the open wound, there is sometimes a stinging which may last 5 to 15 minutes. For this reason, it should be applied before the anesthesia obtained prior to operation has worn off. Its anesthetic action will then last so long that reapplication of eucupin can be made before anesthesia from the first application has worn off. Cotton does not stick to the wound as does gauze, at the time of reapplying fresh eucupin. The cotton soaked with eucupin should be pressed into the wound for 5 full minutes and then left in the wound. It may then be reapplied in the same way every 3 hours for four times. Then the eucupin soaked cotton should be taken out and left out. More prolonged use is unnecessary and may delay healing of the wound.

HEMORRHOIDECTOMY WITH PROLONGED LOCAL ANESTHESIA

It is not to be expected that pain after hemorrhoidectomy can be avoided when the ligature or the various closed, suture operations are performed. In order to make the patient comfortable, the open Pennington operation has here been followed, which dissects out the whole external and internal hemorrhoid down to the sphincter fibers and out in triangles of skin, and then picks up the hemorrhoidal vessels in as small a bite of the hemostat as is possible for double transfixion and ligation. The new operating speculum devised by Fansler makes comparatively easy, this, which is otherwise a difficult, operation.

Spinal or sacral anesthesia is rarely, and general anesthesia never, used. Anesthesia has been obtained by blocking of the branches of the internal pudendal nerves in the ischiorectal fossa. Tutocaine has been used for this purpose because it is twice as potent and about half as toxic as procaine hydrochloride.

In the earlier cases, eucupin 0.1 per cent in physiological saline with adrenalin was in-

filtrated at the close of operation under the wounds. Later nupercaine 0.1 per cent solution in physiological saline with adrenalin, for infiltration was used, fortified by the topical application of eucupin 0.75 per cent solution by the technique heretofore described.

Now, all infiltration by these solutions has been abandoned and eucupin 0.75 per cent in water by topical application to the open wounds by the technique described is used alone. This is usually sufficient. The eucupin thus topically applied has a great added advantage in its powerful bactericidal action which causes it to prevent infection in this field, exposed to contamination.

Clinical results. Stress had been laid on controlled laboratory measurements, because clinical findings can prove the comparative value of these local anesthetics only when very large numbers of cases with very large numbers of controls are available. This is especially true in this rectal problem where patients vary so greatly in their susceptibility to pain. Clinical results given are presented, not as demonstrations, but as suggestive: After 100 rectal operations, patients were told that they could have as much narcotic as they pleased—usually morphine or codeine. Of these, 14 wanted one dose of narcotic, 13 wanted more than one dose, while 73 did not want any narcotic at all. This makes 87 per cent who were free or nearly free from serious pain for the 3 days after rectal surgery! Of these, a few had barbiturates the night after operation to prevent restlessness and most had barbiturates before operation. Three radical operations for internal and external hemorrhoids were performed in the office under local anesthesia. To each of these patients a prescription for codeine was given. Two of the three never had the prescriptions filled as they had no need for the codeine. Another patient, seen in the hospital 7 hours after a radical hemorrhoidectomy, complained strenuously because he was kept in the hospital saying: "I feel perfectly well. I want to get up and walk home!"

SUMMARY

1. An improved method for measuring local irritation by local anesthetics was used in 1,300 tests. The highest concentrations which can be used without sloughing were determined for nupercaine, eucupin, quinine urethane. Similar tests were made of tutocaine hydrochloride, procaine hydrochloride, benacol, anucaine, nupercaine in oil, diothane, and quinine urea dihydrochloride. Vuzin proved more irritating than eucupin.

2. Topically applied in the open wound by a technique described, eucupin 0.75 per cent solution gave excellent results after operations for anal fistula, pilonidal sinus, and hemorrhoids. It may also be applied to prolapsed strangulated gangrenous hemorrhoids. Its bactericidal qualities in addition to its prolonged anesthetic action enhances its value in rectal wounds subjected to contamination.

3. After 100 rectal operations in which prolonged local anesthetics were used, narcotics were offered freely to all, but 73 per cent of the patients were so free from pain that they wanted no narcotic.

4. A solution of quinine urethane not in the concentration used in varicose veins proved the best of these solutions for injection treatment under anal fissure.

APPENDIX

DEATHS FROM NUPERCAINE

Toxicity of nupercaine: clinical

Deaths from spinal injection—
- Hechenbach, W. Ztschr. f. urol. Chir., 28: 295. .010
- Jones, W. H. Quoted by Arnheim and Mage, Lancet, 1930, 219: 549. .0075
- Steinbruck, M. Zentralbl. f. Chir., 1930, 57: 273. .014
- Arnheim and Mage (Weinstein). Surg., Gynec. & Obst., 1932, 54: 826, 2 c. cm. of 1:200. .010
- Keyes and McLennan. Am. J. Surg., 1930, 60: 1 .010
- Idem., J. Am. M. Ass., 1931, 96: 2085. .010
- Ibid. .010
- Ibid. not stated

Deaths from intraperitoneal injection—
- Mandl, F. Zentralbl. f. Chir., 1930, 57: 2966. .150 c. cm. of 1:1000
- Idem. Wien. klin. Wchnschr., 1929, 42: 1393.

Deaths from topical application—

Nose—
- Muenchen. med. Wchnschr., 1929, 76: 2009.

Urethra—
- Tinnin, F. Samml. Vergiftungsfallen, 1932, 3: 215. 10 c. cm. of 1.5 per cent

Bladder—
- Keyes and McLennan. Am. J. Surg., 1930, 9: 1. amount not stated

Infiltration—
- Freund. Klin. Wchnschr., 1929, 8: 1444 .130 c. cm. of 1:1000

Kuehnel. Ugesk. f. Læger, 1931, 37: 924
.....110 c. cm. of 1:1000
Dalsgaard. Ugesk. f. Læger, 1931, 41: 1006
.....120 c. cm. of 1:1000
Siebner. Quoted by Keyes and McLennan (loc. cit.).
Chirurg, 1929, I: 1113..... 90 c. cm. of 1:1000
New and Non-official Remedies, 1937, p. 53
.....135 c. cm. of 1:1000
Medico-Legal. J. Am. M. Ass., 1933, 100: 45
..... 1:1500
Hirschfelder and Bieter. Physiol. Rev., 1932, 12: 236
.....15 c. cm. of 1 per cent
Keyes and McLennan. Am. J. Surg., 1930, 9: 1
.....380 c. cm. of 1:1000
Ibid.....not stated 1 per cent (by mistake)
Ibid.....not stated 10 per cent (by mistake)
Ibid.....80 c. cm. of 1 per cent (by mistake)
Idem. J. Am. M. Ass., 1931, 96: 2086
.....20 c. cm. of 2 per cent

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A NOTE ON PRIMARY SHOCK

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THE proper evaluation of the several etiological factors commonly thought to underlie primary shock is of considerable clinical importance. The interrelation of these factors has been discussed too frequently to warrant recapitulation here. For a recent summary of the subject the reader referred to an article by Walter Cannon. It seemed that one bit of evidence might be obtained from a study of the systemic effects of local tissue damage in an animal isolated, physiologically, from the traumatized tissues.

The literature upon parabiosis, vascular parabiosis, and crossed circulation was reviewed, beginning with Paul Bert's account of his *greffe animale*. No record was found of a satisfactory application of these to the study of shock.

Vaccarezza, in a study directed toward reaching a better understanding of the effects of tissue injury of several sorts, performed the following experiments, using dogs as experimental animals and chlorasol for anesthesia. In a series of experiments, the skin of one leg, from claws to "two finger breadths above the femorotibial articulation" was subjected to thermal injury. The result was physiological collapse and death within 10 hours. Then, by leaving intact the nerves to the extremity and clamping the vessels supplying and draining it, he was able to mitigate these effects. Finally, he established a vascular union between two subjects in such a fashion that blood perfusing the traumatized extremity of one animal was returned to the systemic circulation of the other. The technique was as follows: after treating the leg of one animal, A, Vaccarezza injected physiological salt solution through the femoral artery until it was returned clear via the corresponding femoral vein. An anastomosis was then carried out between this femoral artery and the carotid artery of a normal animal, B. In this way blood from the uninjured animal B irrigated the leg of A. Since the femoral nerve was left intact, the injured extremity had nervous connection with animal A and vascular connections with the healthy animal B. In the two experiments performed, the uninjured animals died, in 5 and 8 hours, while the traumatized animal lived. It was noted that the circulatory exchange persisted only "a few hours," due to the fact that blood coagulated and occluded the anastomoses.

The evidence from these experiments contributed to the author's conclusion that "the cause of shock and death in these cases is due exclusively to the influence of toxic products which, originating at the site of trauma, are carried by blood vessels and lymphatics to the general circulation."

Several criticisms of the foregoing suggest themselves. In the first place, the experiments were not controlled. The history of crossed circulation experiments suggests that evidence thus obtained must be based upon carefully controlled conditions. The thromboses that occurred at the anastomoses in addition to terminating the experiments for all practical purposes, indicate the existence of another pathological process, in itself capable of producing death through embolism. In addition, death may follow anesthesia alone, or, as we later found, may occur from pulmonary lesions incident to the prolonged immobilization under anesthesia. Finally, the absence of necropsy reports leaves one somewhat in doubt as to the actual causes of death.

Since the findings have been quoted by other investigators in spite of these possible objections, and inasmuch as they seemed a particularly pertinent contribution, we decided to repeat and extend the work.

EXPERIMENTAL PROCEDURE

Large animals were selected and paired for equality of weight. With one exception,

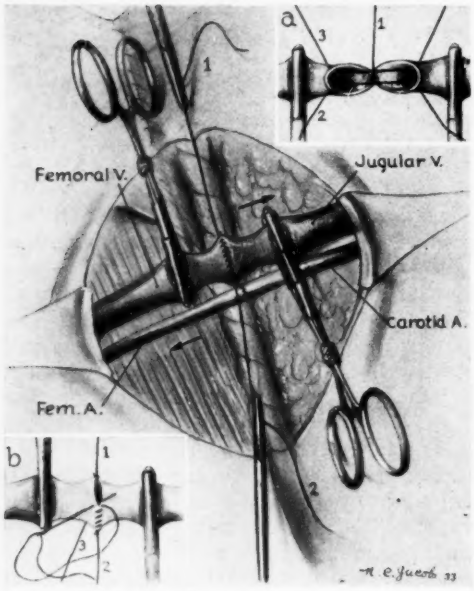

Fig. 1. Details of the operative procedure used in experiments 13 and 14, and in controls. The anastomoses, *a*, *b*, follow the familiar Doerfler-Carrel-Guthrie technique. The posterior wound edges have been united.

the extremity of the heavier subject was used.

After preparation of the left hind leg and thigh of one, animal A, and the neck of the other, animal B, each animal was given an intravenous injection of 0.5 gram of sodium amytal in 10 per cent solution. The skin was prepared with iodine and alcohol, and the adjacent skin surfaces posterior to the sites of incision were brought together with a continuous suture. Small amounts of ether were administered from this point to the completion of the operation. It should be stated definitely at this point that anesthesia was complete and effective throughout all experiments.

An incision was made to the left of the midline of the neck of animal B and through this the jugular vein and common carotid artery were exposed and liberated from surrounding tissues. These then were coated with sterile mineral oil, returned to their beds, and lightly covered with gauze moistened with warm physiological salt solution.

A left inguinal incision served to expose the proximal ends of the femoral artery and vein of animal A. Branches of the artery and tributaries to the vein in this region were ligated to avoid the possibility of a vascular "shunt," and the vessels were freed from surrounding tissues, the femoral nerve being carefully protected. The vessels were then coated with mineral oil and overlaid with moist sponges. A continuous silk suture was employed to bring together the posterior portions of both wounds.

The leg of animal A was then treated from the claws to points 4 centimeters above the femorotibial articulation anteriorly and 6 centimeters above this articulation posteriorly, the Vaccarezza technique being used. Next, the femoral artery and vein of animal A were divided high in the groin, between clamps. By means of a bulb syringe with a drawn out and rounded tip, the vascular bed of the extremity was washed out rapidly with warm salt solution, the injection being made under moderate pressure into the artery, and continuing until only bloodtinged solution came from the free end of the vein. These vessels were caught gently in rubbershod clamps, lubricated and protected by moistened gauze while the carotid and jugular vessels of animal B were divided high in the neck.

The anastomoses were then carried out, the carotid artery of animal B being united with the femoral artery of animal A, and the femoral vein of animal A with the jugular of animal B; so that blood leaving the systemic circulation of animal B traversed the vascular channels of the leg of animal A and returned to its original source.

The operative procedure and the method used in the anastomoses are illustrated in Figure 1. The unions were accomplished by the familiar Doerfler-Carrel-Guthrie technique in which, after the placing of three "guy" sutures (Figure 1a) a continuous suture of fine, lubricated silk, piercing all coats, is employed to bring the edges into end-on approximation (Figure 1b). The drawing also shows the anastomoses running in front of the suture line uniting the posterior portions of the two incisions. Upon completion of the anastomoses, this suture was continued

TABLE I

Maneuver	Controls		Experiments	
	11	12	13	14
Weight of A	22.9 k	29.1 k	22.7 k	22.6 k
Weight of B	22.5 k	23.3 k	22.7 k	22.7 k
Anesthetic	:00	:00	:00	:00
Operation	:40	:35	1:00	1:00
Trauma	None	None	2:00	2:15
Anastomoses functioning	2:55	2:50	3:25	3:30
Division	12:10	12:05	12:05	11:50
Fate of A	Recovery	Recovery	Killed	Killed
Fate of B	Recovery	Recovery	Recovery	Recovery

The salient data of the two experiments on thermal trauma (Nos. 13 and 14) and the two control procedures (Nos. 11 and 12). Time intervals are given in minutes and hours, the experiments being presumed to begin with the administration of the anesthetic.

in such a fashion as to unite the skin edges of the two wounds entirely around the vessels—a tube effect.

With the completion of the operation, ether was discontinued, animal B was rolled toward animal A, and the two turned completely over. This, as will be seen, was found an important part of the technique. Care was taken to support the head of animal B in such a manner that there could be no interference with the circulation of the leg of animal A. Other precautions were taken to this same end. In all experiments, this leg remained warm, and phenolsulphonphthalein, injected intramuscularly into animal A, was found in quantity in the urine of animal B.

It was planned to terminate the experiments after 8 hours, this period equaling the longest survival of animal B in Vaccarezza's experiments. However, the anastomoses actually functioned 8 hours and 40 minutes and 8 hours and 25 minutes in the 2 experiments. The animals were given continuous nursing attention. Small doses of morphia and rare whiffs of ether sufficed to keep them soundly asleep.

At the conclusion of the experiments, the anastomoses were examined (on the "A" side of the arterial union and "B" side of the venous) by inspection, palpation, filling tests, and finally by escape of blood "beyond" the points of union. In every case the anastomoses were found to be functioning competently. After tying the vessels and removing the connecting portions for examination, animal A was killed. The wound of animal B was sutured in layers with fine silk, and this animal was returned to its cage.

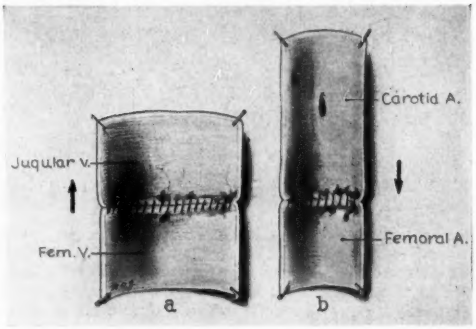

Fig. 2. The carotid-femoral and jugular-femoral anastomoses from experiment 14 after 8 hours of function. This situation accurately represents those found in examinations of the other suture anastomoses. Natural size.

In the two experiments the B animals recovered promptly.

There was no wound infection. The condition of the opened vessels shown in Figure 2, a drawing from the specimens in experiment 14, was typical of the group.

In the two control experiments the anesthesia and operative procedures were identical with the above. Both animals in each set of partners survived. The anastomoses functioned briskly, and the same examination tested their freedom from thrombosis. At the conclusion of these procedures the A animals were not killed. The wounds of both partners in the crossed circulation preparation were sutured with fine silk, and the 4 recovered promptly, without infection or other untoward sequelæ. These experiments were terminated in each case after the anastomoses had functioned 9 hours and 15 minutes. Table I presents the essential data of the foregoing.

In two additional experiments the leg of animal A was subjected to mechanical trauma produced by blows with a blunt instrument, under full anesthesia. This was carried out rapidly and vigorously, and the

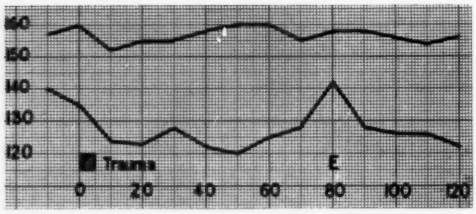

Fig. 3. Graphs of systolic blood pressures in experiments 15 and 16, in millimeters of mercury. Time is in minutes. The elevation at *E* was quite apparently due to a short period of administration of ether. Pulse rates rose very gradually from 120 a minute to 152, and from 121 to 150 in experiments 15 and 16, respectively, during this experimental period.

subsequent very marked edema of the tissues suggested that it had been effective. Because the experiments were of shorter duration, and because earlier effects were anticipated, several minor changes in technique were introduced. Intraperitoneal pentobarbital sodium (50 milligrams a kilogram) was used for anesthesia; anastomoses were carried out preceding the traumatization; Payr cannulas were used in effecting the anastomoses. Continuous blood pressure records of animal B were made, the cannula being inserted into the femoral artery. The experiments were allowed to continue 2 hours after traumatization. In other respects the technique of the two groups of experiments was the same.

Anastomoses were functioning competently at the termination of the experiments, according to the criteria herein given, and phenolsulphonphthalein, injected intramuscularly into the leg of animal A following injury, appeared in quantity in the urine of animal B. At the end of the experiments the A animals were killed; the B animals were returned to their cages.

The blood pressure levels of the B animals showed a slight decline during and shortly after trauma, possibly due to loss of blood into the vascular bed and tissues of the leg of the A animals. Thereafter the blood pressures returned to relatively high levels in both experiments, where, with minor fluctuations, they remained. The pulse rates rose, very gradually from 120 a minute to 152 in experiment 15 and from 121 to 150 in experiment 16. Neither B animal showed other

TABLE II

Maneuver	Experiments 15	16
Weight of A	18.6k	23.8k
Weight of B	17.7 k	22.8 k
Anesthetic	:00	:00
Operation	1:05	:30
Anastomoses functioning	2:40	2:40
Trauma	3:11	3:15
P.S.P.	3:17	4:05
Termination	5:11	5:20
Fate of A	Killed	Killed
Fate of B	Recovery	Recovery

Significant data of experiments 15 and 16 on traumatic shock. Time intervals are as in Table I. "P.S.P." indicates injection of phenolsulphonphthalein.

evidence of primary shock. Both recovered, and 24 hours later gave no obvious evidence of secondary shock. The essential data of these experiments are given in Table II, and graphs of the blood pressure levels are given in Figure 3.

METHOD

Considerable difficulty was experienced before we were satisfied with the method—enough to make us somewhat skeptical of the results in Vaccarezza's two uncontrolled procedures. Ten preliminary experiments, with and without traumatization, were carried out. Though the results in these did not weaken the final experimental conclusions, they showed that deaths may be expected from pulmonary lesions presumably incident to the long immobilization and from some anesthetic agents when used for protracted periods. We found two points in technique worthy of observation. In regard to anesthesia: when using sodium amytal intravenously in experiments of this duration it seems best to use an amount sufficient only for introductory narcosis, and to use morphia and ether for subsequent anesthesia; pentobarbital sodium probably is more satisfactory than sodium amytal. Second, immobilization in one position should be limited to periods of 4 hours.

Several general remarks based upon our review of parabiosis, vascular parabiosis, and

crossed circulation may be in order. Though the technique of parabiosis is the easiest of the three to carry out, the method has other pitfalls. Conclusions, to be convincing, should be based upon a number of experiments. When the time element is introduced, the relationship of the significant maneuver should be cleared of all doubt. For, as Dragstedt and others have pointed out, unexplained deaths, not associated with characteristic lesions and quite unpredictable, are not uncommon.

The crossed circulation techniques are more difficult to carry out and require, on the part of the experimenter, a very clear concept of the problem in hand. Some of the experiments noted so far departed from the comparison to the physiological state that analogies drawn from them are of doubtful validity. Doubt surrounds other results because of the failure of the authors to offer evidence that circulation was in progress during the experiment. Finally, in at least 2 cases, adaptations of the method were used which were far too crude to justify significant conclusions.

In general, we feel that parabiosis is best adapted to the study of effects that are relatively subtle, that are progressive, and that take place over a period of days or weeks. Vascular parabiosis and crossed circulation, on the other hand, seem best adapted to experiments of short duration in which relatively gross changes are anticipated.

CONCLUSION

Two varieties of trauma affecting the leg of one animal perfused by the blood of a second failed to evoke evidence of shock in the second animal. This result tends to derogate the postulate that a lethal toxin is formed in traumatized tissues.

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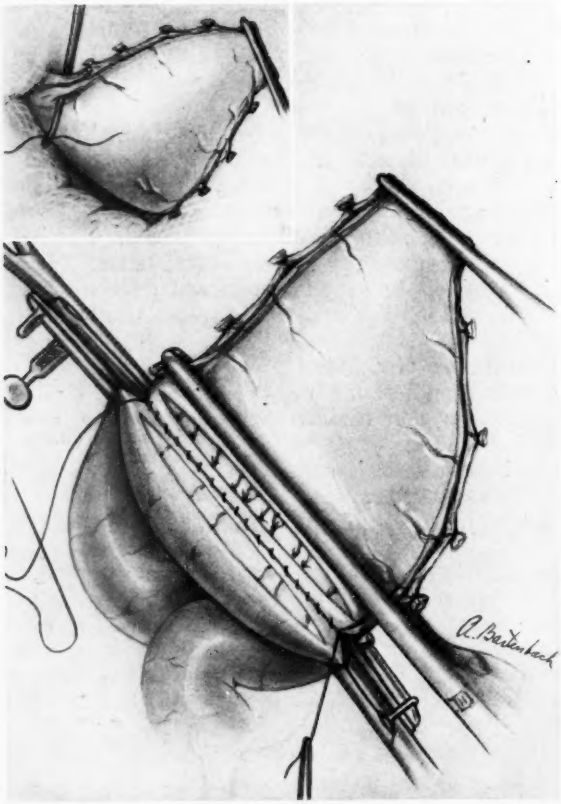

Fig. 5. The insert shows the stomach pulled downward and deflected over the left costal arch so as to expose the left gastric artery which is ligated and cut. The stomach and jejunum are fixed in position by two Lane intestinal clamps, and a continuous catgut seromuscular suture unites the posterior wall of the stomach to the jejunum. The serosa and muscularis of the posterior wall of the stomach are cut and the vessels in the submucosa are ligated.

Technique of Gastrectomy.—Karl A. Meyer.

CLINICAL SURGERY

FROM THE DEPARTMENT OF SURGERY, NORTHWESTERN UNIVERSITY

TECHNIQUE OF GASTRECTOMY

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GASTRIC resection today offers the only curative procedure for malignancies of the stomach. Although, theoretically, total extirpation of the stomach is probably the operation of choice, this procedure is associated with too high a mortality to be of practical value. Subtotal gastric resection with the removal of the greatest possible portion of the stomach and of the surrounding tissue, such as the lesser and gastrocolic omentums and the lymph glands in these structures, gives the best results. In the advanced cases, in which the malignancy has invaded the liver, transverse mesocolon, transverse colon, anterior abdominal wall and pancreas, gastric resection is only a palliative procedure; it removes an ulcerating, bleeding, or obstructing tumor, relieves pain, but does not give a permanent cure or appreciably lengthen life.

There are many types of gastric resection, the descriptions of which are beyond the scope of this paper. The operation that has given us the best results is the Pólya modification of the Billroth II. The technique of the Billroth II, as carried out in our practice, will be discussed and the pre-operative and postoperative care briefly summarized.

PRE-OPERATIVE TREATMENT

The amount of pre-operative treatment depends upon the general condition of the patient and the type of gastric malignancy. From the point of view of pre-operative management, the gastric lesions may be divided into two groups: (1) stenosing tumors which produce pyloric obstruction and gastrectasis, (2) tumors which do not produce obstruction. The stenosing tumors lead to a gastric dilatation, retention of food, hypertrophy, and edema of the gastric wall. These effects of the obstruction can be overcome by lavage of the stomach to free it of food residue and by constant aspiration through a Levine tube for several days. During this period the patient's water balance is maintained by the daily administration of 3,000 to 4,000 cubic centimeters of 5 per cent dextrose in Hartmann's solution, by intravenous drip. The non-obstructing tumors do not lead to these stomach changes and do not require this gastric decompression. Patients are allowed liberal amounts of high carbohydrate, non-residue foods and a large amount of liquids. If a marked anemia is present, blood transfusions are indicated before operation.

ANESTHESIA

The choice of anesthesia in patients with gastric malignancies, especially if associated with loss of weight and debility, is of importance. Patients who are in fair general condition are given a combination anesthesia of avertin (tribrom-ethenol) in doses of 70 to 80 milligrams per kilogram body weight, supplemented by ethylene or 1 per cent novocain local infiltration. Emaciated patients with possible kidney damage are better operated upon under morphine-scopolamine analgesia and local infiltration of 1 per cent novocain and supplemented with ethylene when necessary.

OPERATIVE TECHNIQUE

The operative technique for gastrectomy may be divided into various steps, such as (1) abdominal incision, (2) determination of operability, (3) mobilization of stomach, (4) gastro-intestinal anastomosis.

The abdominal incision most suitable for gastrectomy is the left paramedian incision. However, if the lesion is located high on the fundus or cardia of the stomach, the exposure through this incision may be inadequate. In these cases the operation is facilitated by enlarging the paramedian incision with a transverse incision across the left rectus and extending to the lateral abdominal muscles.

Fig. 1. The index and middle fingers are inserted through an opening in the gastrohepatic omentum and by blunt dissection separate the posterior wall of the stomach from the transverse mesocolon.

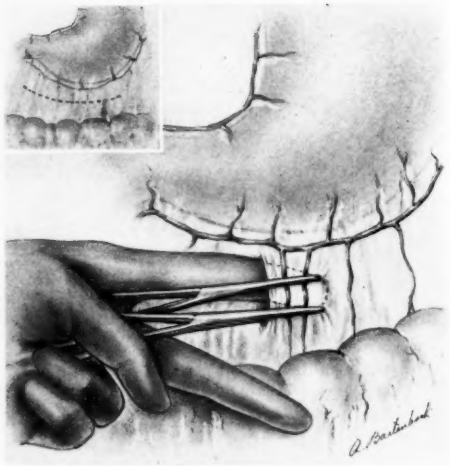

Fig. 2. The gastrocolic omentum is cut between clamps and ligated. The fingers of the left hand separate the gastrocolic omentum from the mesocolon.

Once the abdomen is opened the first factor to determine is operability. If the lesion is not adherent to the anterior abdominal wall, liver, or pancreas, the stomach and transverse colon are lifted up and examined for adhesions between the stomach and transverse colon, or transverse mesocolon. If the transverse mesocolon is invaded by the tumor, the involvement of the middle colic artery is determined. If this artery can be spared, the mesocolon can be resected with the stomach without interfering with the blood supply of the transverse colon. An opening is made in the gastrocolic and gastrohepatic omentums and the posterior surface of the stomach is inspected for adhesions to the mesenteric vessels, transverse mesocolon, and pancreas. If the tumor extends toward the right, the right lobe of the liver is drawn aside and the gall bladder, common duct, and surrounding structures are explored. If the lesion is limited to the stomach and there are no metastases or extension of the malignancy to the surrounding structures, resection may offer a cure. If there is local extension of the mass or metastases to the regional lymph glands, resection is palliative.

If the lesion is resectable, the first step in the technique is mobilization of the stomach. This is accomplished by inserting the index and middle fingers of the left hand through an opening in the gastrohepatic omentum and by blunt dissection separating the posterior wall of the stomach from the transverse mesocolon (Fig. 1). The gastrocolic omentum is then divided between forceps (Fig. 2) and doubly ligated. If the lymph glands are involved, the ligation is done as close as possible to the transverse colon. The division of the gastrocolic omentum is first done toward the cardia and continued toward the pylorus. In the region of the antrum, the gastrocolic omentum is adherent to the mesocolon and can be separated by blunt and sharp dissection, care being taken not to injure the vessels of the mesocolon, especially the middle colic artery. If the lesion has invaded the mesocolon and separation is impossible, the diseased portion of mesocolon must be excised. If the middle colic artery is injured, the adjoining colon must be resected with the stomach. As the separation approaches the pylorus, two peritoneal folds are seen passing from the hepatic flexure of the colon to the duodenum and pylorus, one passing to the right and one to the left. The right fold contains the right epiploic artery and vein which are severed between forceps and ligated. The left fold leads to the pancreas and contains many small branches of the gastroduodenal artery and vein. These vessels, although they are small in size, are cut between forceps and doubly ligated. By this procedure the duodenum is gradually freed from the head of the pancreas.

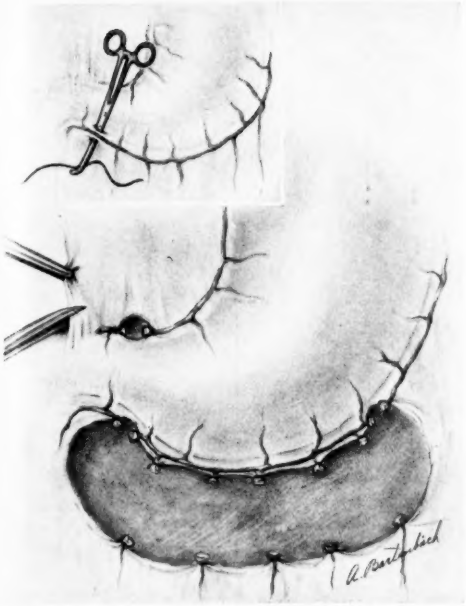

Fig. 3. The gastrocolic omentum is cut and the vessels ligated. The gastro-epiploic and pyloric (right gastric) arteries are ligated and cut.

The next step in the mobilization of the stomach is division of the gastrohepatic omentum. The stomach is now brought down and to the left so as to bring the duodenum and lesser omentum into view. Beginning at the opening in the gastrohepatic omentum through which the fingers were placed to mobilize the posterior surface of the stomach, the gastrohepatic omentum is cut between forceps and ligated. This mobilization is carried downward toward the duodenum. In the hepatoduodenal ligament there are many small vessels which are carefully isolated, cut between forceps, and ligated. After the duodenum is mobilized, it is divided between two Payr clamps (Fig. 4), care being taken to protect the surrounding tissues from contamination. The proximal stump of duodenum is covered with a lap sponge and the distal stump is closed. Closure of the duodenal stump is an important step in the procedure of gastrectomy and failure of adequate closure has resulted in many unfortunate postoperative sequelæ. The stump is closed by a continuous silk suture which, beginning at one end, grasps a fold of serosa and muscularis on one side a short distance below the forceps; then the suture is carried over the forceps and a similar stitch is taken on the

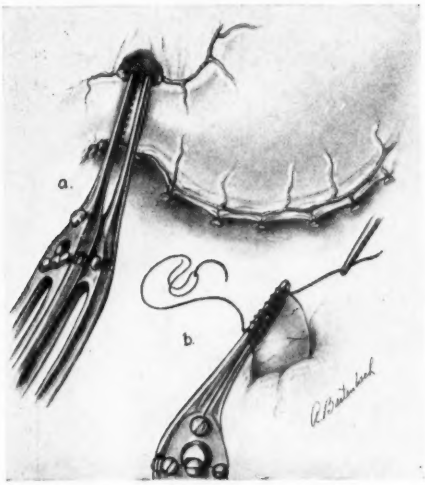

Fig. 4. Two Payr clamps are placed close to each other in the first portion of the duodenum and the bowel cut between them. The duodenal stump is closed by a continuous basting suture running over the Payr clamp. As the clamp is removed the suture is pulled taut and inverts the crushed end of the duodenum.

other side of the duodenum and then back over the forceps to take a stitch on the first side and so on until the other end is reached. As an assistant slowly removes the clamp, the operator pulls the two ends of the suture taut. This procedure closes and folds in the cut edges of the duodenum. Without tying the ends of the suture, the operator places an interrupted Lembert suture at each end of the duodenal stump and the free ends of the continuous suture are then tied to the Lembert suture. A row of interrupted Lembert sutures are placed over the first suture line. The suture line may be further reinforced by a third layer of interrupted Lembert sutures or by covering it with omentum or capsule of the pancreas.

Further mobilization of the stomach is accomplished by dividing the gastrohepatic omentum toward the cardia. The stomach and duodenum are pulled downward so as to stretch the attachment of the gastrohepatic omentum to the lesser curvature. At a point close to the gastric border the omentum is cut between forceps and doubly ligated, applying two ligatures on the side toward the cardia on account of the tendency of the vessels in the fatty infiltrated omentum to slip. The branches of the coronary artery which radiate from the gastrohepatic omentum to the anterior and posterior walls of the stomach are cut between forceps and ligated. During this

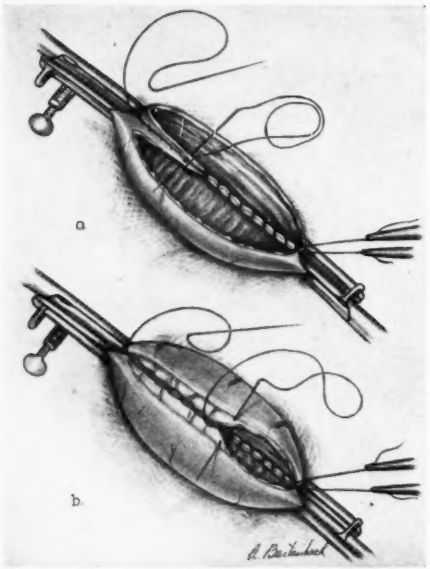

Fig. 6. a, The stomach is amputated and a continuous catgut suture passes through all the layers of the stomach and jejunum uniting the posterior wall of the stomach to the jejunum. b, As the suture reaches the lesser curvature it is carried over to the anterior wall as a continuous suture through the mucosa. At the greater curvature the suture is tied to its short end.

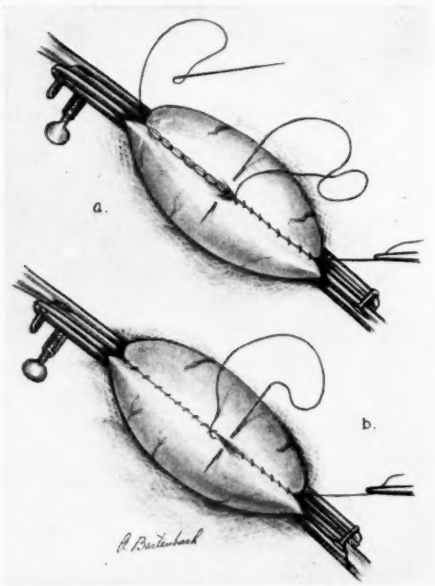

Fig. 7. a, The mucosal suture described in Figure 6 is continued back as a continuous seromuscular suture and tied to the seromuscular suture of the posterior wall and cut, leaving the posterior suture intact. b, The posterior seromuscular suture is continued over the anterior portion of the anastomosis as a third layer suture.

procedure the lesser curvature of the stomach is freed of its peritoneal covering. The stomach is now lifted up and turned back over the left costal arch so that the posterior surface may be inspected. The gastrosplenic ligament, vasa brevia arteries, and adhesions are cut between forceps and ligated.

The fourth step in the procedure of gastrectomy is the performance of the gastrojejunal anastomosis. The stomach, which has been extensively mobilized, is brought down from beneath the costal arch and grasped with a Lane intestinal clamp as high as possible above the tumor and the redundant stomach reflected over the left costal arch so as to make the posterior surface easily accessible. The first loop of jejunum is brought through an opening in the transverse mesocolon, and is approximated to the posterior wall of the stomach so that it runs from lesser to greater curvature in an antiperistaltic direction (Fig. 5, opposite p. 611). The segment of jejunum between the stomach and duodenojejunal angle is made as short as possible without causing too much traction on the suture line. A second Lane intestinal clamp is applied to the jejunum which is approximated to the posterior wall of the stomach and the forceps are fixed in position. The jejunum is attached to the posterior wall by a continuous Lembert catgut suture. After the completion of this suture, the distal segment of stomach is clamped and amputated about 1 centimeter from the Lembert suture. The jejunum is then opened about 0.5 centimeter from the Lembert suture. The cut edges of the posterior wall of the stomach and jejunum are sutured with a continuous over and over suture grasping all three layers, (Fig. 6). This suture is started at the greater curvature and progresses toward the lesser curvature. When the anterior wall is reached, instead of grasping all three layers, only the mucosa is sutured along the anterior wall. When the greater curvature is reached, the ligature is tied to the short end, and is then reversed, grasping the serosa and muscularis of the anterior wall of the stomach and jejunum (Fig. 7). When the lesser curvature is reached, this ligature is tied to the continuous seromuscular suture of the posterior wall and is then cut, leaving the posterior suture

with its attached needle intact. The clamps are now removed. Following this, the posterior seromuscular suture is continued along the anterior wall as a third layer suture. The entire suture line is reinforced with interrupted silk Lembert sutures. Along the lesser curvature of the stomach where the stomach has been freed from its peritoneal covering, the anterior and posterior walls are approximated by interrupted Lembert sutures, thereby burying the deperitonealized area of the lesser curvature.

The suture line is now drawn through the opening in the mesocolon (Fig. 8). The stomach is attached by interrupted Lembert suture to the edges of the opening in the mesocolon. If the remaining stomach is short, it may be impossible to pull it down through the opening in the mesocolon. In these cases, the opening may be closed around the loops of jejunum.

The abdominal incision is closed without drainage of the peritoneal cavity. The incision is closed with interrupted sutures in three layers. Catgut is usually used in the posterior sheath of rectus, transversalis fascia, and peritoneum which are taken as one layer and in the anterior rectus fascia. Interrupted silkworm is used in the skin. In debilitated patients with poor healing properties, interrupted silk sutures may be used throughout all layers.

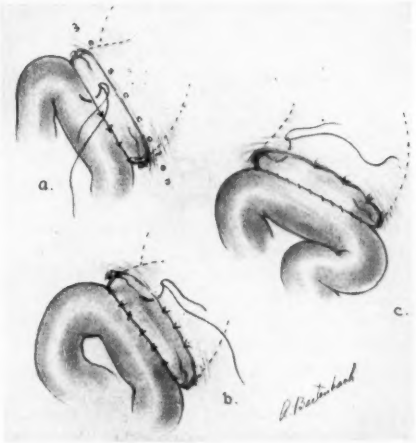

Fig. 8. a, The anastomosis is reinforced with a layer of interrupted Lembert sutures. b, The posterior wall of the stomach is sutured to the mesocolon by interrupted sutures. c, The anterior wall of the stomach is sutured to the mesocolon.

POSTOPERATIVE TREATMENT

Immediately after the operation a blood transfusion is given. Following this, transfusions of blood are repeated as conditions warrant. During the first 4 or 5 days, the stomach is kept decompressed with a Levine tube and constant suction. During this period the water balance is maintained by the administration of 3,000 to 4,000 cubic centimeters daily of 5 per cent dextrose in Hartmann's solution. About the fifth or sixth day the Levine tube is clamped off and fluids are given orally. If the fluids are tolerated, the Levine tube is removed and the diet is gradually increased.

The general postoperative care is essentially the same as that of any laparotomy patient. He is encouraged to change position in bed and to sit in a semi-recumbent position in order to avoid pulmonary complications.

Patients with a malignancy have poor healing properties so that it has been our practice not to remove the tension sutures of the abdominal incision for at least 2 weeks, and, if the patient is emaciated, they are left in as long as 3 weeks. Many eviscerations may possibly be avoided by using this precaution.

RETRO-ESOPHAGEAL GOITER

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RETRO-ESOPHAGEAL goiter, while not a surgical rarity, is sufficiently unusual to warrant a report of 4 cases. The object of this discussion is, first, to place on record these case histories, and, second, to show that this anatomical variant of goiter constitutes a definite clinical entity which, with the aid of a few simple laboratory examinations, may be accurately diagnosed before operation.

It has not been an uncommon experience, especially with adenomatous goiters, to find at operation, small projections of thyroid tissue lying in the tracheo-esophageal groove, or in the cleft between the esophagus and the vertebral column. Failure to visualize these masses, due to incomplete delivery of the thyroid lobe, is undoubtedly responsible for the many so called "recurrences" following thyroidectomy for adenomatous goiter. However, it is not this variant of goiter to which I refer in this paper. The variety encountered in the following cases has passed, in its growth, mesially from the postero-internal aspect of the thyroid lobe across the midline between the prevertebral fascia and the posterior surface of the esophagus.

It is probable that the factor influencing the growth of retro-esophageal goiter is similar to that which determines the development of a substernal goiter; the direction of growth is in the line of least resistance. In the initial enlargement of the gland, the greatest bulging usually occurs anteriorly and laterally. However, after the goiter has become large, the pretracheal muscles become more or less unyielding and further growth may occur in the direction of least resistance, either substernally or along the fascial plane behind the esophagus. As Pemberton points out, the relative greater frequency with which retro-esophageal goiters are encountered in secondary operations for recurrent disease may be explained by the fact that the tissues anteriorly and laterally are unyielding because of the presence of scar tissue. However, it seems more likely that in the so called recurrent cases, these projections do not develop subsequent to operation but were overlooked by the surgeon who failed to dislocate the thyroid lobe completely. The absence of adhesions and the ease of delivery of the retro-esophageal projection, in one of the described cases, would seem to corroborate this viewpoint.

A well defined retro-esophageal goiter will invariably cause symptoms which, if carefully analyzed, will be found to be out of all proportion to any obvious anterior and lateral thyroid enlargement that may be present. In our 4 cases herewith reported, all complained of attacks of choking, brought on especially when turning the head to the side opposite to the point of entrance of the goiter in the retro-esophageal space. This was more evident with the patient in the reclining position. One patient developed attacks of dyspnea which were relieved by inclining the head toward the affected side. This was corroborated by the findings at operation. One patient complained of frequent spells of coughing which came on invariably after retiring at night. Assuming an upright position often brought relief. A sense of constriction in the neck was noted by all the patients. One patient complained of difficulty in swallowing which, however, was not constant. In 1 instance, the overlooked retro-esophageal extension was a factor in the continuation of severe thyrotoxic symptoms. The outstanding symptom in 2 instances was hoarseness which was variable in intensity and duration. The most recent patient disclosed a paralysis of the right vocal cord on the same side of entrance of the retro-esophageal goiter.

It may be extremely difficult to make a diagnosis of retro-esophageal goiter on the basis of physical signs alone. If the antetracheal portion of the goiter is definitely enlarged, a clinical diagnosis may be impossible. If the thyroid isthmus is insignificant, the finding of anterior displacement of the trachea, especially against the upper manubrial edge, should cause the surgeon to suspect a retro-esophageal extension. In the most recent case, it was possible to palpate the trachea pushed forward by a large adenoma, which could be moved from left to right behind the esophagus. In 1 of the 4 cases, the abnormality was not suspected before operation. In the 3 remaining instances, the retro-esophageal position of the goiter was diagnosed clinically.

In attempting to seek a more graphic method of depicting the presence of a retro-esophageal goiter before operation and to fortify the clinical diagnosis by some exact method, in 1933 I had a lateral roentgenogram of the neck made on the third case reported here. This film indicated a

well defined anterior displacement of the trachea. Then, in order to outline the position of the esophagus in relation to the trachea, the goiter, and the vertebral column, another lateral roentgenogram was made at the moment of swallowing a mouthful of barium. This clearly delineated the displacement of the esophagus by a mass behind its posterior surface. The X-ray films of the fourth case, (Fig. 5), disclosed, in addition, a narrowing of the upper esophagus by the posteriorly placed adenoma. I believe that these 2 methods of X-ray examination are valuable aids to the surgeon in arriving at a pre-operative diagnosis of retro-esophageal goiter.

At operation, removal of the retro-esophageal projection may offer little difficulty. If this portion of the goiter is large, the danger of injuring the recurrent laryngeal nerve is real. In 2 of the reported cases, it was possible to roll out the posterior projection while dislocating the major portion of the lateral lobe and to remove it with the remainder of the goiter. In the 2 other cases, this maneuver was impossible. Realizing the danger of recurrent nerve injury, I resected the major part of the lateral lobe leaving the retro-esophageal portion *in situ*. All severed vessels were then tied so as to free the operative field of clamps. A temporary ligature was then placed about the inferior thyroid vessels in order to control bleeding from its branches. The posterior portion of the goiter was then dissected out of its bed in a practically bloodless field, without endangering the integrity of the recurrent nerve or parathyroid bodies.

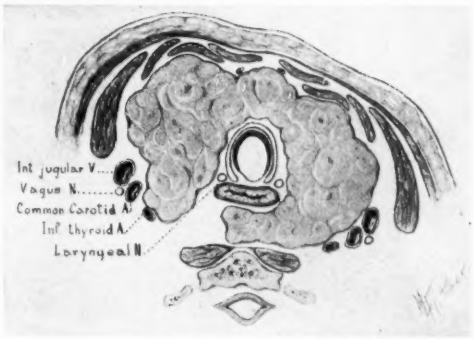

Fig. 1. Cross section of the neck showing diagrammatically the retro-esophageal extension in Case 1. The relative position of the recurrent nerves and inferior thyroid vessels should be noted.

CASE REPORTS

Case 1. Mrs. L. H., aged 53 years, was first seen on November 15, 1928. She complained of a goiter of 20 years' standing, with recent increase in size, especially on the right side. For the preceding 4 years, she had noted increasing nervousness, palpitation, and a loss of 30 pounds in weight. She also complained of choking sensations which were aggravated by turning the head toward the left side in a reclining position. In addition, she had the sensation of constriction about the neck.

Examination showed an elderly woman, quite nervous. There was no exophthalmos. There was moderate dental caries. The heart was somewhat enlarged to the left and was totally irregular. Pulse deficit amounted to 20. Pulse rate was 160. Blood pressure, systolic 170; diastolic 90. Laryngeal examination was negative. She was admitted to the New York Hospital on November 26, 1928. Laboratory tests revealed a negative urine, a negative Wassermann, and a normal blood count. Basal metabolic rate on November 20, 1928, was plus 83 per cent. Following rest in bed; the administration of Lugol's solution; a high caloric diet; etc., the patient's basal metabolic rate dropped to plus 51 per cent within 10 days.

Operation was performed on December 14, 1928. Because of the large size of the goiter, the pretracheal muscles were divided transversely. There were numerous adenomas, some solid, some cystic, extending into the lateral recesses of the neck and partly beneath the sternum. Great difficulty was encountered in attempting to dislocate the right lobe. It was finally determined that this was due to a large adenoma which passed posteriorly between the esophagus and vertebral column (Fig. 1). The right lobe and isthmus were partially resected and the bleeding points were ligated. A temporary ligature was then placed around the inferior thyroid vessels and, by a combination of sharp and blunt dissection, the retro-esophageal mass was finally dislocated into the wound and removed. The recurrent laryngeal nerve was never visualized. A subtotal resection was then done on the left side; the adenoma, which had grown down behind the manubrium, was removed.

After operation, this patient did well. Laryngeal examination on the fourth day after operation was negative. The pathological examination of the removed goiter disclosed numerous adenomas with some hyperplasia. The patient was discharged with the wound completely healed on the twelfth day after operation. The basal metabolic rate was plus 2 per cent. She has remained well to date.

The follow-up on this patient is extremely interesting. She developed, 1 year later, signs of an abdominal tumor which, upon operation, proved to be actinomycosis of the transverse colon. This was reported in the *Annals of Surgery*, 1934, 99: p. 531.

Case 2. Mrs. H. S., aged 36 years, referred by Drs. W. Klingman and E. Hauser, was first seen October 2, 1933, at which time she complained of a goiter of 6 months' duration. She stated that for the preceding year, she had been troubled with a persistent cough which became more evident at night after retiring. These coughing spells were productive of a small amount of mucus. In addition, she experienced frequent attacks of hoarseness which did not respond to therapy and which spontaneously subsided after a day or two. For the past 5 or 6 months, she had been conscious of a sense of constriction about the neck. The attacks of coughing at night time were relieved when she assumed an upright position. In addition, she presented symptoms of mild thyrotoxicosis; palpitation, nervousness, dyspnea on exertion, mild exophthalmos, a loss of 5 pounds, and tremor.

Examination showed a well developed young woman, troubled with a persistent dry cough. The skin was moist. There was slight exophthalmos, and the thyroid gland was uniformly enlarged and soft. The lateral borders could not

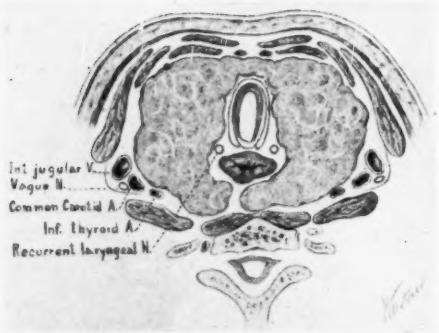

Fig. 2. Cross section of the neck to show bilateral retro-esophageal extensions of the goiter described in Case 2. The position of the various anatomical structures are indicated.

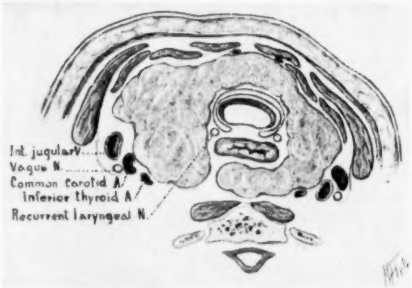

Fig. 3. Cross section of neck. Case 3, showing the retro-esophageal projection of the right lobe of the thyroid which was responsible for persistence of hyperthyroid symptoms in addition to the mechanical effects of the mass.

be definitely demarcated. Laryngeal examination revealed normally functioning vocal cords. The heart was negative. Pulse was 128. Blood pressure was: systolic 122, and diastolic 84.

She was admitted to the New York Hospital on October 2, 1933, where further study revealed a basal metabolic rate of plus 18 per cent, negative urine, and negative blood examination. An X-ray examination of the chest showed no substernal projection of the goiter. The probability of a retro-esophageal extension of the goiter was suggested before operation.

Operation was performed on October 6, 1933. Through the usual collar incision, the thyroid gland was exposed and found to be moderately enlarged. It was filled with numerous small adenomas, varying in size from 1 to 3 centimeters in diameter. The isthmus was divided and an attempt was made to deliver the right lobe. It was soon evident that there was present, a projection of thyroid tissue posteriorly between the esophagus and vertebral column. A finger inserted into this groove met resistance on the left side. It was found that the left lobe also presented an extension posteriorly which almost met the right sided projection behind the esophagus (Fig. 2). It was possible in this case to enucleate the projection on each side and to perform a subtotal resection of each lobe. The right recurrent laryngeal nerve was visualized. The left nerve was not seen.

Examination of the removed thyroid lobes showed numerous adenomas with scattered areas of hyperplasia. Some of the acini showed small papillary projections.

After operation this patient did well. There was immediate relief from the attacks of coughing and the patient very quickly lost the sensation of cervical constriction and choking which she complained of before operation. Post-operative examination of the larynx revealed normally functioning vocal cords. Since then the patient has done well.

Case 3. A. F., male, aged 41 years, was first seen on October 27, 1933. He stated that for the preceding 2 years, he had experienced frequent attacks consisting of a sensation of constriction about the neck, choking, marked "pounding of the heart" and tachycardia, which gave him the feeling of impending dissolution. Immediately preceding these attacks, he noted difficulty in breathing upon inclining his head toward the left side. About 8 months before, he observed an enlargement of the thyroid gland. He consulted a physician who advised immediate hospitalization. Further examination revealed a basal metabolic rate of plus 74 per cent, with a hypertension of 280 systolic, and 160 diastolic. In addition, marked cardiac enlargement was noted. After preliminary treatment with Lugol's solution, and other measures, an operation was performed on the thyroid gland at another hospital. The operative notes state that a subtotal removal of the right lobe was done. Patient was confined to the hospital for 2 months after the operation, and then he began to have repeated attacks similar to those he experienced before the operation.

Six months later when I saw him, he presented evidence of a severely toxic Graves' disease with marked psychomotor activity, excessive sweating, nervousness, tachycardia (160) tremor, and weakness. He was admitted to the New York Hospital on November 11, 1933. Further examination revealed the scar of the former thyroid operation and moderate enlargement of the left lobe. The trachea could not be clearly outlined. The heart was greatly enlarged; the left border extending to the anterior axillary line. There was a systolic murmur at the apex. Blood pressure was, systolic 238, diastolic 150. Pulse, 120, was regular. Basal metabolic rate was plus 43 per cent. Urine examination showed albumin, 4+; few hyaline casts. Hemoglobin was 90 per cent; blood Wassermann was negative. Urea nitrogen was 17 milligrams; blood sugar 93 milligrams; uric acid 4 milligrams per 100 cubic centimeters.

Because of the patient's history of choking sensations, of cervical constriction, of relief in the upright position, and also of relief following turning of the head toward the right, a lateral roentgenogram of the neck was made. This showed a forward displacement of the trachea. Another film was made immediately after the swallowing of barium; this indicated a forward displacement of the esophagus by a retro-esophageal mass. A pre-operative diagnosis of Graves' disease with a retro-esophageal extension of the goiter was made.

Pre-operative preparation consisted of the administration of Lugol's solution, high caloric intake, sedatives, etc. The basal metabolic rate dropped to plus 23 per cent. Operation was performed on November 21, 1933. The scar was excised. Considerable scar tissue was found infiltrating the depressor muscles with fixation to the thyroid gland. The gland was finally exposed and was found to present a considerable enlargement of both lobes. In an attempt to dislocate the right lobe after ligation of the superior pole and division of the isthmus, great difficulty was encountered. This was found to be due to a large projection of

Fig. 4. Pre-operative lateral roentgenogram of the neck. Case 4, showing the anterior displacement of the trachea which is caused by the presence of a mass in the retro-tracheal region by a retrotracheal mass.

Fig. 5. Pre-operative lateral roentgenogram of the neck, Case 4, immediately after the ingestion of a barium mixture showing the anterior displacement and angulation of the esophagus by a retro-esophageal mass.

thyroid tissue extending posteriorly across the midline between the esophagus and the vertebral column (Fig. 3). In order to protect the integrity of the recurrent laryngeal nerve, the right lobe was partially resected and bleeding points were ligated. A temporary ligature was placed around the inferior thyroid vessels. By a process of blunt and sharp dissection, the retro-esophageal projection was delivered into the wound. The absence of adhesions in the region, and the ease of delivery of this projection indicated that manipulation at this site had not occurred during the first operation, and that the surgeon had completely overlooked the presence of the retro-esophageal extension. A subtotal resection was performed on both lobes, and the wound was closed.

Pathological examination of the specimen revealed scattered areas of hyperplasia with papillary projections of the acinar epithelium. The patient did extremely well after operation. Laryngeal examination was negative. The basal metabolic rate dropped to minus 5 per cent. The patient was discharged on the twelfth day after operation in excellent condition. Since then there has been no return of the attacks which occurred so frequently before, and the patient has remained well.

I am indebted to Dr. Richard Lewisohn for permission to report this case. This patient was on his service at the Mt. Sinai Hospital recently and was operated upon by him. He recognized clinically the probability of a retro-esophageal goiter and demonstrated the condition by lateral roentgenograms of the neck as already indicated. The clinical diagnosis was confirmed at operation.

CASE 4. S. F., married housewife of 42 years, was admitted to the surgical service of Dr. Lewisohn on February 27, 1935, complaining of the presence of a goiter of 7 years' duration, and hoarseness and dysphagia of 9 months' duration. During the past 7 years, she had noted a gradually increasing swelling in her neck, confined mainly to the left side. Aside from the presence of the swelling, she had no other symptoms until 9 months before admission when she suddenly noted hoarseness. This persisted with varying intensity up to the date of her admission. During this same period, she noted frequent attacks of choking brought on especially after inclining her head toward the left side. Rotating her head again toward the right side relieved the choking sensation. In addition, she noted intermittent difficulty in swallowing.

Examination showed an obese female with facial hirsutism; no exophthalmos. There was a large adenoma occupying the right side of the neck and the isthmus, and a smaller, freely movable, cystic adenoma, in the left lobe of the thyroid. It was possible to palpate the trachea which seemed to be displaced forward by a posterior mass. It was possible to palpate an adenoma which seemed to be attached to the right lobe and pass behind the trachea, and could be moved slightly from side to side. Laryngeal examination revealed a right recurrent nerve paralysis. The right vocal cord was in the midline. There was a small amount of outward motion in the right arytenoid but the cord itself was immobile. The left vocal cord moved normally. Blood pressure was 105 systolic, 70 diastolic. Blood count was negative. Hemoglobin was 90 per cent. The urine was negative. Blood sugar was 95 milligrams. Blood Wassermann was negative. Basal metabolic rate was plus 7 per cent. X-ray examination of the chest showed a moderate degree of diffuse dilatation of the aorta. There was no evidence of intrathoracic goiter. A lateral X-ray of the neck disclosed the trachea pushed forward by a retro-tracheal mass (Fig. 4). Lateral X-ray of the cervical esophagus following the ingestion of barium, showed some constriction of the esophagus and displacement of this organ anteriorly by a retro-esophageal mass (Fig. 5). A diagnosis of multiple non-toxic adenomas of the thyroid with retro-esophageal extension was made.

Fig. 6. Lateral roentgenogram, of same patient taken 6 days after operation. From this picture it is seen that the trachea has returned to practically normal position.

Fig. 7. Lateral roentgenogram of same patient 6 days after operation, following the ingestion of a barium mixture, showing the return of the esophagus to normal position and the correction of the anterior angulation.

Operation was performed by Dr. Lewisohn on March 4, 1935. There was a large adenoma occupying the right lobe. Some difficulty was encountered in completely dislocating the right lobe, due to the presence of a large adenoma measuring approximately 2½ by 1½ inches, extending from the right side behind the esophagus almost across the midline. It was possible to roll this adenoma out of its retro-esophageal position, and to perform partial resection of the right lobe. The left lobe contained a large adenoma which also was removed.

Convalescence was quite uneventful. There was almost immediate relief of practically all her symptoms with the exception of hoarseness. At the time of her discharge from the hospital on the tenth day after operation, laryngeal examination showed the right vocal cord to be immobile. The operative wound had healed by primary union.

CONCLUSIONS

1. Retro-esophageal goiter is a definite clinical entity which may be diagnosed before operation.

2. Characteristic symptoms are sense of constriction about the neck, attacks of choking especially when turning the head away from the side of entrance of the goiter in the retro-esophageal space, spells of coughing, dysphagia, and hoarseness of variable intensity.

3. The probable diagnosis of a retro-esophageal goiter should be kept in mind if it is possible to determine anterior displacement of the trachea against the upper edge of the manubrium.

4. Retro-esophageal extension of a goiter may be graphically depicted by lateral roentgenograms of the neck showing anterior displacement of the trachea, and also after the ingestion of a barium mixture, to outline the position and shape of the esophagus.

5. The operative technique is discussed.

HYPERTROPHIC CRICOPHARYNGEAL STENOSIS[1]

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NEW YORK, NEW YORK

IN the recent literature, attention has been directed to benign disorders of the upper esophagus resulting in dysphagia and malnutrition. This type of dysphagia is usually the result of unstable emotional states, malnutrition, and anemia, especially that form of anemia associated with glossitis, vitamin deficiency, achlorhydria, and splenomegaly. It is generally believed that the upper and lower ends of the esophagus are normally in a state of tonic closure and that the usual cause of benign spastic dysphagia is some neuromuscular dysfunction. At the entrance of the esophagus the comparatively powerful cricopharyngeus muscle is responsible for its tonic closure. Branches of the glossopharyngeal (ninth cranial nerve) and the vagus (tenth cranial nerve), together with some fibers of the cervical sympathetic system, form the pharyngeal plexus, which in turn innervates the constrictors of the pharynx as well as the pharyngeal mucosa. Therefore, the cricopharyngeal muscle is subject to both sensory and psychical stimuli. Any series of sensory stimuli, if continued to a point of causing irritation of the mucous membrane, would therefore set up a vicious cycle, as would also psychical stimuli resulting from severe emotional reactions.

Hypertonicity, spasm, or inefficient relaxation (achalasia) may lead to passive congestion, edema, round cell infiltration, hypertrophy, and degeneration of muscle fibers, and finally, fibrosis. It is significant, however, that long standing so called cardiospasm of the lower esophagus does not lead to muscular hypertrophy of the cardiac portion of the esophagus.

We have had the opportunity of examining and operating upon a patient who presented a benign tumor of the cricopharyngeus muscle due to hypertrophy and degeneration of its fibers, together with intracellular edema, probably as a result of a long standing neuromuscular dysfunction. Our pre-operative diagnosis was incorrect in that we expected to find a parathyroid tumor or an atypical thyroid tumor encircling the esophagus. With the tumor exposed, we believed it to be an inoperable neoplasm and, thinking to afford the patient a certain degree of palliation, carried out what we believe is a new operative procedure. The patient is now alive, well, and symptom free, 20 months after operation. Preoperative data and postoperative follow-up are complete, and as material was obtained for microscopic study, we believe that it is justifiable to report this case in some detail, hoping that our

Fig. 1.

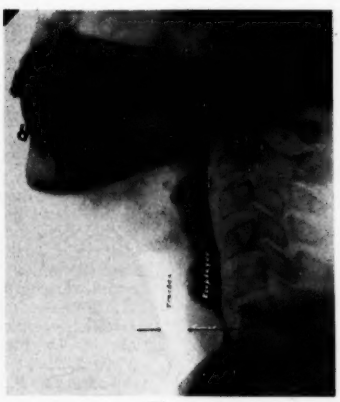

Fig. 2.

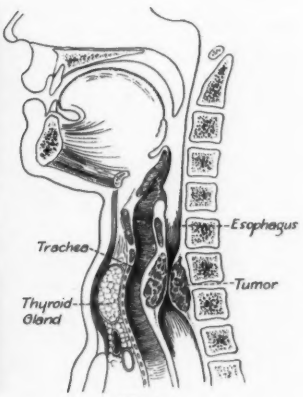

Fig. 3.

Fig. 1. Pre-operative lateral view of the neck showing the smooth mound-like swelling in the midline. It was at first thought to be of thyroid gland origin.

Fig. 2. Roentgenogram showing the smooth funnel shaped narrowing of the esophagus opposite the level of the fifth and sixth cervical vertebræ.

Fig. 3. Diagrammatic sagittal section showing the esophageal obstruction, tracheal compression, and thyroid prominence which were brought about by the post-cricoid tumor.

From the Surgical Service of the Fifth Avenue Hospital, Dr. F. W. Bancroft, Director.

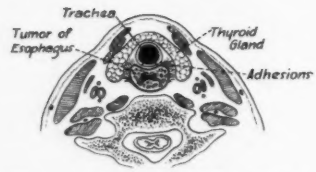

Fig. 4. Diagrammatic cross section of the neck at the level of the esophageal lesion showing its relation to the surrounding structures and adhesions to the thyroid gland and trachea.

observations may be of some help to the surgeon unexpectedly confronted with a similar situation.

The patient, an American housewife, 49 years of age, was first seen at the request of her family physician, February 27, 1933, because a piece of meat had lodged in her upper esophagus necessitating removal by means of a forceps. She gave a history of having noted a "thyroid" enlargement of 6 years' duration, associated with rare attacks of palpitation. She was otherwise well, until 1 year before admission when she noted intermittent dysphagia and a feeling that food stuck at the lower neck level. Six months later, she became definitely unable to swallow meat and it was eliminated from her diet. There had been only slight loss of weight, although the diet was limited to liquids and soft solid foods. She had been nervous and irritable for years and admitted having had a bad temper.

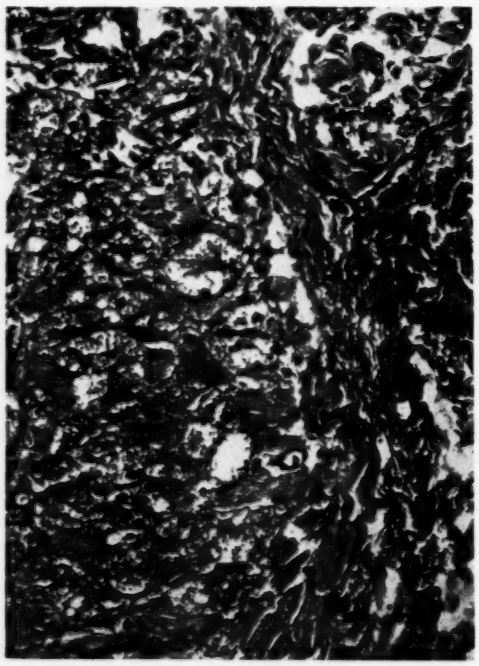

Fig. 6. Photomicrograph of the biopsy material removed at operation. It shows edema and fibrosis together with hypertrophy and degeneration of striated muscle fibers.

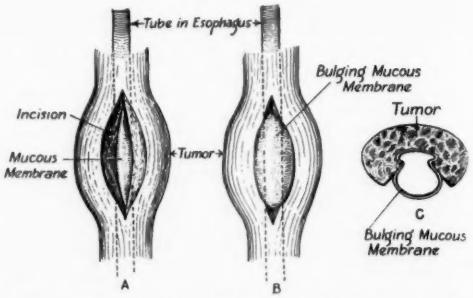

Fig. 5. Operative steps: A, A tube has been placed in the esophagus and a longitudinal incision made through the tumor down to the esophageal mucous membrane. B, The mucous membrane is shown bulging through the incision. C, A cross section showing how the lumen of the esophagus was enlarged by the incision of the tumor down to the mucous membrane.

Examination of the neck revealed a smooth, rounded, mound-like swelling in the midline at the level of the thyroid gland isthmus (Fig. 1). It was diffuse, fairly soft, attached to the underlying trachea; it moved when the patient swallowed and measured 4½ centimeters in its transverse and longest dimension. There was no cervical lymphadenopathy. Intra-oral and laryngeal examinations revealed no abnormality.

Laboratory findings showed: (1) Basal metabolism rates on 2 occasions were —1 and +6. (2) X-ray films taken after the ingestion of a barium meal showed a smooth area of esophageal constriction at the level of the fifth cervical vertebra (Fig. 2). (3) Aspiration biopsy was attempted but the nature of the cells could not be determined. (4) Esophagoscopy was carried out after cocainization of the pharynx with 10 per cent cocaine, and a 9 millimeter esophagoscope was passed readily to the level of the cricopharyngeal constriction, where the instrument met an obstruction due to spasm or extrinsic pressure. The lumen was narrowed considerably and the mucous membrane presented in longitudinal folds and appeared somewhat puckered. Under direct vision a 7 millimeter olive tipped bougie could, with difficulty, be forced through. No definite esophagoscopic diagnosis was made, but it was felt that the esophageal condition was due to extrinsic pressure. (5) Blood count and urinalysis were normal. (6) Further fluoroscopic studies during the ingestion of barium paste showed a narrowing of the lumen of the esophagus at the level of the sixth cervical vertebra, where the barium was seen to pass slightly to the left of the midline. In the lateral direction the narrowing was the same as seen in the anteroposterior direction, and the involvement was over an area of approximately ¾ inch. The trachea showed evidence of posterior pressure. Dr. R. E. Pound, who made the radiographic studies, suggested that the esophageal condition might be secondary to pressure from an enlarged thyroid which had extended around the trachea posteriorly and pressed on the esophagus.

An exploratory operation was decided upon and carried out under intratracheal anesthesia, March 24, 1933. The usual collar incision for a thyroidectomy was done and

A B

Fig. 7. A and B, Postoperative roentgenograms after ingestion of barium, showing the increased width of the esophageal lumen and its lateral position.

both lobes of the thyroid were mobilized. After considerable careful dissection, it was decided that the tumor was inoperable and it was incised longitudinally along its left lateral border down to its mucous membrane which then bulged through the incision. On cut section, it was about 1 centimeter in thickness and it looked and felt like cartilage. A piece of this tissue was removed for biopsy purposes and a frozen section was done. A Levine tube was passed through the esophagus into the stomach. Both lobes of the thyroid were then replaced and a wick of gauze was inserted on each side and a routine closure was done without incident (Figs. 3, 4, 5).

The material removed at operation for microscopic examination was described by Dr. C. Zent Garber as follows: "Macroscopical examination of the specimen removed at operation measured 7 by 3 by 3 millimeters. It was of a yellowish pink color, smooth surfaced, and quite firm. Microscopical examination showed a border of dense fibrous tissue surrounding some small blood vessels. Adjacent to this there was much striated muscle. The fibers stained a dull pink, the cytoplasm was granular, the cell outline poorly marked and the nuclei stained poorly. No tumor cells or inflammatory cell reactions were seen. Further sections showed some degeneration of muscle fibers and some fibrous and adipose tissue."

The postoperative course was stormy and complicated by acute embolic nephritis, right otitis media, right mastoiditis, and an operative paralysis of the left recurrent laryngeal nerve. Her convalescence was slow but she was discharged from the hospital much improved 37 days after the operation.

Postoperative X-ray films after the ingestion of barium paste, have been taken periodically and show (Figs. 7a and b), that the esophageal lumen is somewhat enlarged and is located to the left of its pre-operative midline position. On fluoroscopy the barium is seen to pass through this area without delay.

The patient has made steady progress and is now robust and healthy. The neck mass has largely disappeared (Fig. 8). Her voice is somewhat less husky, although the left side of the larynx is still partially paralyzed. She eats a full diet without any difficulty.

Fig. 8. Postoperative photographs of neck.

SUMMARY

Our findings, operative procedure, and results, bear a striking similarity to the condition which Rammstedt first described in reporting his operation for congenital hypertrophic pyloric stenosis.

Bougienage in this case was attempted but the pathological condition found at operation showed clearly why adequate stretching of this area would not have been possible.

The procedure described has not been reported previously as far as we have been able to learn from a review of the available literature.

NOTE.—Dr. James B. Woods of Tsingkiangpu General Hospital, China, in a personal communication, states that he has seen a number of his Chinese patients who, after a prolonged fit of temper, absolutely uncontrolled, show definite symptoms of stricture of the esophagus. In a number of cases this symptom persists and if untreated some of these patients die of dehydration and starvation while others pass over into a chronic type of esophageal stricture where fibrosis has taken place to a greater or lesser degree. For want of a better name the condition is known in China as "anger disease."

COMBINED ONE STAGE CLOSED METHOD FOR THE TREATMENT OF PHARYNGEAL DIVERTICULA[1]

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WITHOUT using too many cumbersome definitions and boring classifications, the writer, nevertheless, deems it necessary to arrange pharyngeal diverticula in definite groups based on the literature to which he has had access and on his personal operative experience in 79 cases. Clarity of definition usually promotes the advancement of any subject. The time has come for more accurate classification of the so called "pulsion esophageal diverticula," which really arise in the pharynx and should therefore be named, accordingly "pharyngeal diverticula." There are no recorded cases of true pulsion diverticula of the esophagus. The cases recorded as diverticula of the esophagus arise either opposite the bifurcation of the trachea or at the lower end of the esophagus. They are not pulsion in origin but result from peri-esophageal inflammation and are, therefore, traction diverticula. They are mentioned here to emphasize their difference in etiology from the pulsion pharyngeal diverticula.

HISTORY OF PHARYNGEAL DIVERTICULA

These diverticula are usually incorrectly termed in the literature "esophageal" (Killian, Jamison, and Moynihan). There is no doubt that credit for the first observation of pharyngeal diverticula belongs to Mr. Ludlow. He furnished illustrations and an accurate description of this then unknown condition to Dr. William Hunter in the year of 1764. Later descriptions were made by Monroe in 1811, and by Sir Charles Bell in 1816. The name of Mattheu Baillie is also associated with an early description of this condition.

About 1850 Kluge had the idea of extirpating the sac. Nichaus in 1884 was the first to extirpate the sac.

The common method of treatment had been by bougies. As early as 1848, Dendy attempted to obliterate diverticula by means of caustics. In 1871, electricity in the form of faradization was used by Waldenberg. It is now obvious that since the year of 1848 these pharyngeal pouches were not as common as we have been led to believe. Furthermore, it would seem that some of these ancient plans of conservative treatment have survived even to the present day.

The postmortem examination of Whitehead's patient reported in 1891 showed that the pharyngeal pouch consisted of all three coats of the pharynx, and was observed at the junction of the pharynx and the esophagus. This is contrary to the belief that all of these pouches arise as herniations of the mucous membrane. While it is difficult to believe that a hernial sac can contain all of the musculature which makes up the parent structure, the writer has had a similar case. In the reporter's case, the wall of the sac consisted of all of the coats of the pharynx. The pouch, however, did not arise from the junction of the esophagus and the pharynx, but at a much higher level from the lateral wall of the pharynx.

While S. J. Mixter, in 1894, had cut into one of these pouches and had removed enough of the sac to make the esophagus a straight tube from the "spur" up, his operation was apparently not one of deliberate extirpation of the sac. After reading both reports carefully, the writer believes that the operation performed by W. Joseph Hearn in 1896 and reported in 1899 was the first deliberate extirpation of the sac in the United States. Hearn's operation was performed in the Jefferson Hospital.

Girard, of Berne, in 1896, deeply impressed by the mortality of the operations that had preceded his two cases, devised a technique with which to invaginate the sac without opening into the esophagus. This method of treating the sac has

[1] The preliminary report of this paper was read before the Philadelphia County Medical Society on March 22, 1932, DaCosta Night (in honor of Dr. John Chalmers DaCosta)

been used by Albert Edward Halstead, J. B. Murphy, A. D. Bevan, and others.

Henry T. Butlin's contribution in 1898 added very little to that already promulgated by his predecessors. His technique did not differ from Barrow's technique except that he used silk sutures instead of catgut.

In 1900, Richardson reported a plastic operation on the esophagus below the pharyngeal pouch. The writer can find no other recorded cases in which this procedure was found necessary.

A distinct contribution to this subject was by A. Bois Barrow in 1905. Barrow used a bougie in the pouch during the course of the operation. This does not differ in principle from our present plan of treatment except that we now use the esophagoscope instead of the bougie in order to facilitate identification of the pouch. Barrow's method of treating the neck of the pouch does not differ from our present plan. He reflected back the muscle at the neck of the sac and ligated the mucous membrane inside of the reflected cuff; then, by stitching over the muscles of the hypopharynx, he buried the ligated mucous membrane.

Since these early cases, many operations for the cure of pharyngeal diverticula have been advocated. These operations may be classified as the one and two stage operations. Here, nothing but extirpation of the pouch is considered because the writer has performed no other operation for the cure of pharyngeal diverticulum.

It is the belief of the reporter that all operations of extirpation of the sac were one stage procedures until 1910 when C. H. Mayo performed and advocated extirpation in two stages in order to avoid the possibility of a neck infection descending into the mediastinum. The technique of the two stage operation was developed by E. S. Judd and C. H. Mayo until the latter, in 1923, could report 74 two stage operations with but 3 deaths. The two stage operation has been adopted by Charles Gordon Heyd, Frank H. Lahey, Eugene H. Pool, and by many others.

Lupke, in 1921, reported that he had operated upon 39 cases by the one stage method of extirpation of the sac. There were 2 deaths: 1 from mediastinitis; 1 from hemorrhage.

In the last analysis, the surgeon must be guided by his own experience. Thus far the writer has had no reason to abandon the one stage operation. Bensaude, Grégoire and Guénaux, in 1922, in discussing the statistics compiled by DeWitt Stetten, note that the mortality between 1900 and 1909 is lower than between 1886 and 1900. These three authors think that the fear of infection of the cellular tissues of the neck and of the mediastinum are without much foundation. These authors have collected 109 cases with one stage operations. In this series, there were 12 deaths of which 3 were caused by septic cellulitis of the neck. In 23 cases, there had been more or less prolonged suppuration of the peri-esophageal cellular tissue. These complications became rarer as operative technique improved (Bensaude, Grégoire and Guénaux).

Moynihan, in his scholarly analysis of this subject in 1927, has insisted that these pouches are from the pharynx and should be called "pharyngeal."

THE SITE OF ORIGIN OF PHARYNGEAL DIVERTICULA

For many years it had been almost universally accepted that pharyngeal diverticula arose from Laimer's triangle. This belief persisted until 1908, when Killian wrote his epoch making article on the anatomy of the esophagus and pharynx. Killian, not being satisfied with the previous dissections done by Luschka and later on by Laimer, resolved to study the region of the hypopharynx and the esophageal orifice.

Much of Killian's labor had gone for naught until Sir Berkeley Moynihan investigated the subject in 1927. In his article, Moynihan corrected the erroneous belief that pharyngeal diverticula arose from Laimer's triangular area. He pointed out that Laimer's triangular area is situated below the lower border of the cricopharyngeus muscle of the pharynx. He emphasized the fact that diverticula did not arise in Laimer's triangular area by stating that there were no recorded cases originating in this area.

Killian further demonstrated another possible area for the origin of the pharyngeal diverticula. He showed the presence of a defect below the cricopharyngeus muscle. He called this defect a slit. This slit is below the cricopharyngeus muscle and above the esophageal fibers. Killian's description is as follows: "The slit that we see on each side between the pars fundi-formis and the circular fibers of the esophagus is a very important area. Here in this slit the recurrent nerve passes through to divide into the anterior and posterior branches." Killian makes no mention of this area in its relationship to diverticula of the pharynx. It is quoted here because of the work recently reported by Moynihan on dissections made by J. K. Jamison. It is because of this original work, done by Killian and confirmed by Moynihan, that we are attempting to establish in this series of cases the relative frequency of this site for the origin of pharyngeal diverticula.

Fig. 1. Double diverticulum as shown by X-ray plate.

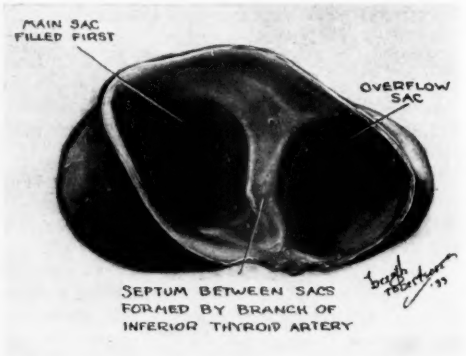

Fig. 2. Gross specimen of pharyngeal diverticulum which has bifurcated by a branch of the inferior thyroid artery.

Killian's studies demonstrated that the lowermost bundle of the inferior constrictor muscle, which he calls the sling bundle of the pars fundi-formis, is the chief closing muscle of the esophageal opening. In the state of contraction it presses the opening of the esophagus together and holds it against the cricoid plate, thereby producing a crescent shape with the concavity forward. In his text and by photograph, he further points out the influence of the cricopharyngeus muscle in the production of pharyngeal diverticula.

The observation of Jamison, while not original, certainly has crystallized our knowledge of the subject. He observed not only the inferior branch of the recurrent laryngeal nerve, but also a branch of the inferior thyroid artery and vein and a bundle of lymphatics passing through this hiatus. This anatomical observation of Killian and Jamison explains the symptom of hoarseness which was present in 9 of our patients. Likewise, it explains the presence of hoarseness which temporarily followed 2 of our operations. A curious fact concerning the postoperative hoarseness was that it was not apparent immediately after operation but came on gradually after the fifth day. The hoarseness in both cases, fortunately, entirely disappeared.

That this slit is not an uncommon site for the origin of a diverticulum is further emphasized by the frequent presence of a branch of the inferior thyroid artery crossing the fundus of the sac. We have had occasion to ligate this vessel in at least 35 per cent of our cases. We believe that the deformity of the fundus of the sac, as shown by X-ray pictures (see Fig. 1), is caused by the entrance of a branch of the inferior thyroid artery into this slit. If this be so, this supposedly unusual site of origin for diverticula would prove to be a common one for the origin of pharyngeal diverticula.

The presence of a double diverticula (see Fig. 2) could be explained by the presence of a larger branch of the inferior thyroid artery which was too resistant to yield with the sac and consequently bifurcated the opening at the neck of the sac. Indeed, it is our belief that a diverticulum can arise from any portion of the pharynx which is perforated by a branch of the inferior thyroid artery (see Fig. 3). This belief is fortified by the origin of a diverticulum much higher than the cricopharyngeus. The defect of the oblique fibers in the posterior lateral wall of the inferior constrictor muscle appeared as though it had been punched out with an instrument. The sac was covered with a thick muscular coat—the only diverticulum in this collection which had a muscular covering. The X-ray and bronchoscopic studies confirmed this high origin of the sac. Dr. Manges reported, "a rather large diverticulum originating a little higher than the average, apparently just below the larynx." Because of the unusual covering, and high origin, I performed a two stage operation. The second stage consisted not only of the removal of the sac but also of the repair of the pharyngeal defect.

Briefly, true pulsion diverticula have been observed by us to originate in one of three areas: (1) They have arisen most frequently, in our experience, from the commonly described area above the cricopharyngeus muscle, either on the left or on the right side; more frequently on the left. In 4 of our patients the pouch originated

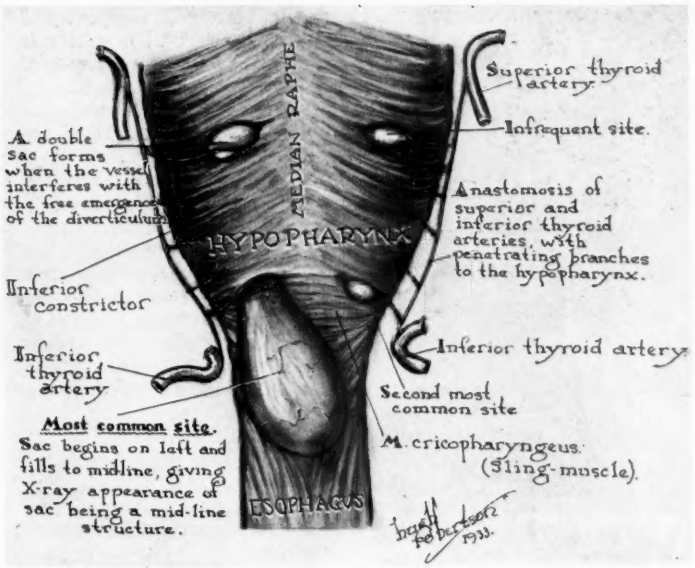
Superior thyroid artery
Infrequent site.
A double sac forms when the vessel interferes with the free emergence of the diverticulum
MEDIAN RAPHE
HYPOPHARYNX
Anastomosis of superior and inferior thyroid arteries, with penetrating branches to the hypopharynx.
Inferior constrictor
Inferior thyroid artery
Inferior thyroid artery
Second most common site
Most common site.
Sac begins on left and fills to midline, giving X-ray appearance of sac being a mid-line structure.
M. cricopharyngeus. (Sling-muscle).
ESOPHAGUS

Fig. 3. The pharynx, posterior view showing the various locations for the development of diverticula.

from the right side of the pharynx. (2) The next place in the order of frequency for the origin of the diverticula in this series, was the Killian-Jamison area. This is on the posterolateral wall of the pharynx, below the cricopharyngeus and above the circular muscle fibers of the esophagus. Through this weak area the inferior laryngeal nerve, a branch of the inferior thyroid artery and a bundle of lymphatics pass. In this area more than 35 per cent of the pouches arose. (3) The location least frequent for the origin of the diverticula has been through the lower portion of the inferior constrictor muscle, a site for another branch of the inferior thyroid artery.

PHYSIOLOGY

It would seem that some other factor or factors, aside from the neuromuscular co-ordination of the pharynx and the esophagus, must be considered in a careful analysis of the physiology of swallowing. The act of deglutition differs for liquids and for solids. The phenomena observed in swallowing liquids is manifested by a rapid rise of pressure within the pharynx, which is almost instantly followed by a projection of the liquids with great force into the esophagus. Second, in the course of swallowing solid food, there is a temporary arrest of the bolus of food in the pharynx. The further passage of solid food depends upon the action of the constrictors of the pharynx. Analyzing these two accepted physiological facts, it would seem that a ready explanation for the beginning of herniation in the pharynx is found in the muscular weakness at one of the vulnerable points already described. Once begun in this manner, the further progress of the herniation is stimulated by each act of swallowing of liquid.

By experiment it has been demonstrated that at the beginning of deglutition there is a sudden rise of pressure, the result of a quickly acting force resident in the mouth or pharynx, in consequence of which the liquid foods are rapidly shot down toward the end of the esophagus, peristalsis playing no part in the process. The proof of these statements was furnished by Meltzer. It was found as a result of many experiments by the aid of esophageal and pharyngeal balloons connected with tambours, that the pharyngeal and esophageal pressure was simultaneous when liquids were swallowed. From this it was inferred that liquids were projected or shot down. The pharyngeal and esophageal balloons are both compressed at the same instant.

These facts demonstrate that deglutition consists of two phases:

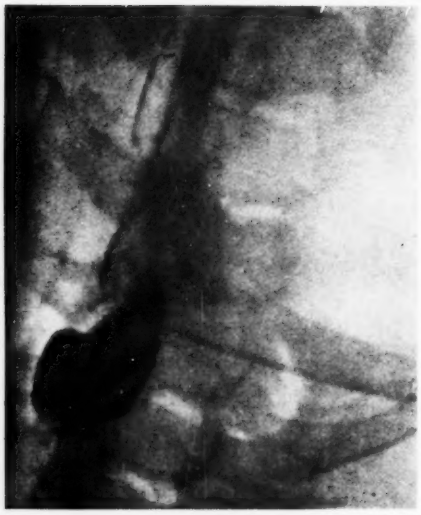

Fig. 4. Malignant diverticulum. Showing the existence of carcinoma in a pharyngeal diverticulum. A distant pouch with irregularities in its base.

1. A rapid rise of pressure in the pharynx, as a result of which, liquid or semi-liquid foods are suddenly shot down to the lower end of the esophagus.

2. A peristaltic contraction of the musculature of the canal, which, acting as a supplementary force, carries onward any particles of food in the canal and forces the bolus through the esophagogastric orifice which is now opened by a relaxation or inhibition of the sphincter cardiac muscle.

The immediate cause of the sudden rise of pressure was shown by Meltzer to be the contraction of the mylohyoid muscles. These muscles are probably assisted in their action by the contraction of the hyoglossus muscles as well as the tongue itself.

SYMPTOMS OF DIVERTICULA OF THE PHARYNX

1. Dysphagia is the most common symptom of diverticula of the pharynx. The dysphagia varies from absolute inability to swallow liquids or solids to a relatively small degree of inconvenience in swallowing. In the beginning, when the pouch is small, the individual is able to swallow after the pouch is filled; but, as the pouch increases in size, it frequently assumes a position between the esophagus and the vertebral column, so that, when the pouch is filled, it presses on the lumen of the esophagus to such a degree as to render swallowing utterly impossible.

2. Vomiting is a prominent symptom. Regurgitation of food from a partially filled sac is frequently an annoying condition. This varies from immediate regurgitation, as soon as the sac is partially filled, to regurgitation a number of hours after eating. Indeed, stagnated food, regurgitated at night, often produces chronic bronchitis. In fact, one of the first symptoms complained of by the patient is regurgitation of undigested food mixed with saliva.

3. Many patients complain of noisy deglutition. This symptom is commonly so annoying as to cause the patient to eat alone. A number of patients of the writer never ate in the presence of others or in public. One patient waited to eat until the rest of the family had dined.

4. Hoarseness is not an uncommon symptom. Nine patients in this series complained chiefly of hoarseness.

5. A tumor, occasionally, in the neck may be palpated. This sign was present in 5 patients of this series. Invariably a gurgling sensation could be detected beneath the fingers, when the patient swallowed.

While the symptoms described, when present, are helpful in leading one to suspect the presence of a diverticulum, the diagnosis is invariably made during X-ray or fluoroscopic examination. While the report of the roentgenologist's findings may usually be accepted as conclusive, uncertainty arose in 3 cases of this series, because of distortion of the fundus of the sac (see Fig. 4). The question was settled conclusively by the esophagoscopist. One patient had a carcinoma in a pharyngeal pouch, another had a pharyngeal diverticulum. Subsequently, resection of the hypopharynx and cervical esophagus showed a carcinoma in the fundus of one sac. This patient lived for 3 years following the operation. The other sac was distorted by adhesions and a branch of the inferior thyroid artery and was not malignant.

PROGNOSIS

The question of mortality in diverticulum of the pharynx has undergone a revision in recent years. Now diverticula of the pharynx are recognized early. The sac does not reach the dimensions that were observed in our early series of cases, consequently, now, the patient's physical condition when operation takes place, is much better than formerly. It was not unusual in our early cases to resort to gastrostomy preceding the operation for diverticulum. (For early procedure, see the original paper by Chevalier Jackson and the author.) We have not done a preliminary gastrostomy on the last 50 patients.

THE MORTALITY OF VARIOUS TYPES OF OPERATION

Much is said, by those who advocate the two stage operation, of the high mortality due to mediastinitis which follows the one stage operation. Where this opinion had its origin, we do not know, nor have we been able to find any record of the high death rate due to mediastinitis in recent years. Certainly, it has not been a complication in any of our 76 cases. We believe that mediastinitis should not occur any more frequently in the one stage operation than in the two stage operation. The easy access to the sac, its rapid separation from the lateral and posterior wall of the esophagus, is only possible when an esophagoscope is in the sac. The esophagoscope is of invaluable aid until the neck of the sac is reached, then it is temporarily withdrawn.

Secondary hemorrhage is often quoted as a complication of the one stage operation. This is without foundation in our experience. We have not had any secondary hemorrhages in any of our pharyngeal diverticula. In 1926, a death occurred due to secondary hemorrhage. This mortality was not in a case of pharyngeal pulsion diverticulum but it occurred in a patient suffering with a traction diverticulum. In this case, part of the pharyngeal wall was purposely resected. This patient is not reported in this series, as it is not a case of pulsion diverticulum.

Recurrence of the sac occurred in 2 patients of this series. In 1 patient, 67 years of age, there was a double diverticulum which involved practically all of the lower lateral pharyngeal wall. We believe that this recurrence could have been avoided if a longer interval than 6 months had elapsed between the removal of the first and second pouch. The second recurrence was in a patient in his late sixties with a very poorly developed musculature of the pharynx. This diverticulum arose from the Killian-Jamison area. Both patients have been re-operated upon by me, and there has been no recurrence in 10 years in the first and 3 years in the second case.

Pulmonary complications not infrequently follow the operation. Many of these patients have a pre-operative bronchitis as a result of overflowing of the contents of the pouch into the larynx. There is a spilling of the foul contents of the sac, usually during sleep, and this infected liquid flows through the larynx into the bronchi, so that clinically, bronchitis is often an associated condition. One of our two fatalities in pharyngeal diverticula was due to a diffuse pneumonia.

Renal complication was responsible for the other death; the patient, 67 years of age, dying of uremia 48 hours after operation.

Fig. 5. Atresia of the esophagus. The barium had been introduced into the lower end of the esophagus through a gastrostomy.

Temporary pharyngeal fistula occurred in 5 of the early cases. This has been obviated in subsequent cases by an improvement in our technique.

Wound infection as a complication has been noted to occur in those patients in whom the omohyoid muscle had been sutured. We now divide the omohyoid muscle only when such division is necessary in order to prevent trauma to the sac during its delivery. When it is necessary to divide the omohyoid muscle, it is not sutured.

We have now considered all the immediate and remote complications associated with our one stage operation.

We believe that the 2 deaths reported in this series might have been avoided if intratracheal ether anesthesia had not been used. We have discontinued its use and have substituted ether anesthesia by rectum. The last case was done under avertin anesthesia.

We are not in accord with those who believe that the two stage operation for diverticula indicates recent surgical progress, because the two stage operation is supposed to eliminate mediastinitis as a postoperative complication. Mediastinitis has not been a complication in any of the 76 one stage operations performed by us.

The writer admits that the two stage operation, as it is done today, far surpasses the older methods of treatment, by eliminating most of the dangers of the one stage operation as it was done in the past. The two stage operation is not logical, because, inasmuch as the diverticulum is a hernia of the pharynx, no effort is made in the two stage operation to repair the pharyngeal defect. This operation simply removes, in the first stage, the redundant sac, and, in the second procedure, the secreting mucous membrane of the remaining portion of the sac. The very basis of the cure depends upon: traction on the pharynx which frequently distorts this structure as well as the upper portion of the esophagus; obliteration of the pha-

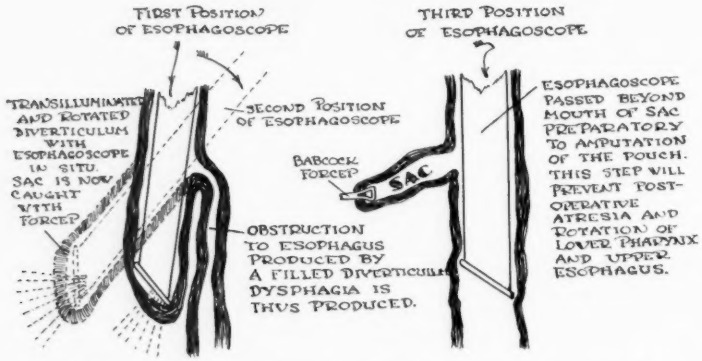
FIRST POSITION OF ESOPHAGOSCOPE
THIRD POSITION OF ESOPHAGOSCOPE
TRANSILLUMINATED AND ROTATED DIVERTICULUM WITH ESOPHAGOSCOPE IN SITU. SAC IS NOW CAUGHT WITH FORCEP
SECOND POSITION OF ESOPHAGOSCOPE
BABCOCK FORCEP
SAC
OBSTRUCTION TO ESOPHAGUS PRODUCED BY A FILLED DIVERTICULUM. DYSPHAGIA IS THUS PRODUCED.
ESOPHAGOSCOPE PASSED BEYOND MOUTH OF SAC PREPARATORY TO AMPUTATION OF THE POUCH. THIS STEP WILL PREVENT POST-OPERATIVE ATRESIA AND ROTATION OF LOWER PHARYNX AND UPPER ESOPHAGUS.

Fig. 6. Diagram showing internal manipulation by the esophagoscopist.

ryngeal opening at the neck of the sac by scar tissue, rather than by surgical repair, as is done in the one stage operation.

One writer cautions those who contemplate doing the two stage procedure of the strong probability of entering the sac during the dissection necessary for the separation of the sac from the esophagus; again he warns the operator of the probability of entering the sac while freeing it at the neck; again he cautions the operator not to enter the sac while suturing it to the muscles in the incision. If he accomplished the delivery of the sac and its fixation without perforation, other complications may be anticipated. Angulation of the pharynx may cause complete atresia. Necrosis of the sac may follow distention. The necessity of postoperative passage of bougies may ensue for at least a year. With these complications as possibilities and occasional occurrences following the work of one of the great surgeons in this country, any operation for diverticulum of the pharynx should be considered a serious one.

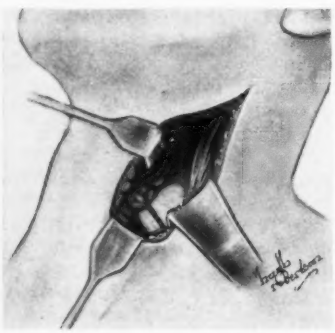

Fig. 7. Showing the incision in the neck and the retracted thyroid gland. The esophagoscope is in the pouch illuminating the fundus. An aberrant vessel is shown crossing the fundus of the sac.

There is no doubt that the two stage operation is the operation of choice: when the surgeon either discards the aid of the esophagoscope; or when the aid of the esophagoscope is not available. This fact is strongly emphasized by the pathetic condition of two patients who were operated on by the one stage operation, without the aid of the esophagoscope. Both of these patients were operated upon outside of Philadelphia. These patients were admitted to the Bronchoscopic Clinic, both had atresia of the esophagus. One had paralysis of the recurrent laryngeal nerve. In one of the patients, a portion of the esophageal wall had been excised and the pharyngeal pouch was not touched (Fig. 5). The X-ray picture shows absolute block of the esophagus. The barium had been introduced into the lower end of the esophagus through a gastrostomy fistula. The writer did a reconstructive operation on the esophagus of each of these patients, with the aid of the esophagoscope, which was introduced through the mouth and the gastrostomy fistula. Dr. Louis H. Clerf assisted in these procedures. Both patients are now swallowing satisfactorily.

We believe that the operation of choice is the one which at its completion leaves the pharynx and the esophagus in their normal positions: not angulated; not stenosed. This operation should not only remove the redundant sac but repair the defect in the pharyngeal wall. In the ideal operation, danger of rupturing the sac, either in freeing it from its bed or separating it at the neck, is reduced to a minimum by the aid of the

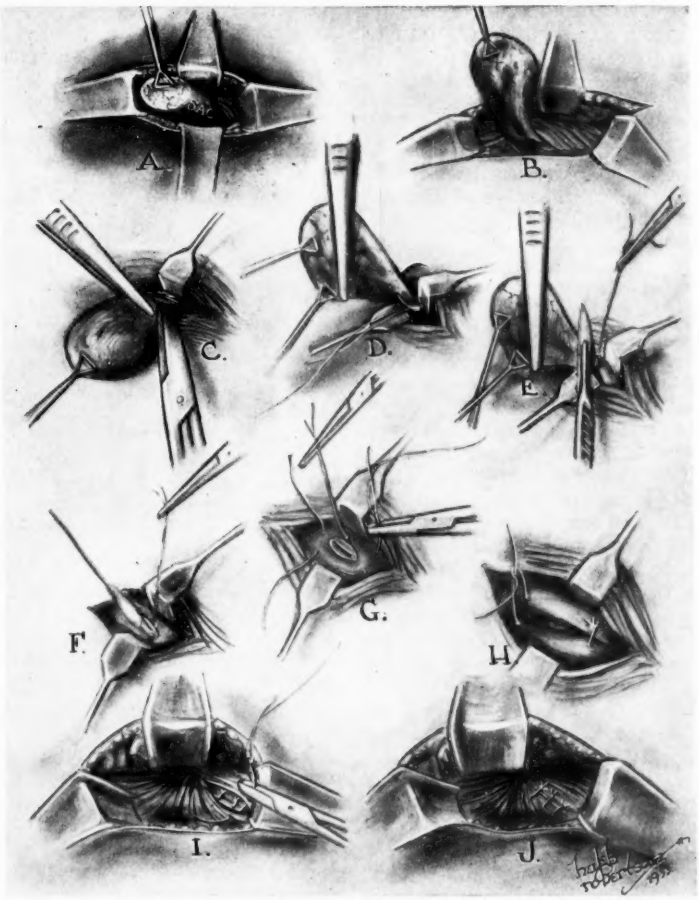

Fig. 8. The various steps in the operative procedure.

esophagoscope (Fig. 6). The operation to be selected is the one which eliminates the risk of penetrating the sac during its fixation to the muscles in the incision. We believe that all of these desiderata are combined in the one stage closed operation with the aid of the esophagoscope.

This procedure was first advocated by Jackson, and he, in conjunction with Gaub, reported 2 cases in 1915. Since then, the writer has entirely modified the surgical technique. The operative procedure which has been described herein is not Gaub's technique, but one which was devised by the writer.

TECHNIQUE AT OPERATION

Under rectal ether anesthesia, intratracheal or avertin, the patient is prepared in the usual manner and an incision is made on the side on which the sac presents and along the anterior border of the sternomastoid muscle (Fig. 7). The incision is to reach from the level of the hyoid bone to 1 inch above the sternum and is to pass through the skin, platysma, and deep fascia, exposing the anterior belly of the omohyoid muscle. This muscle may be divided transversely, or retracted. With this incision the external jugular vein may be exposed, and if it is, it should be divided and tied. The common carotid artery and the internal

jugular vein are now exposed and retracted outward. If the thyroid gland is decidedly enlarged, it is sometimes necessary to ligate and cut the superior thyroid artery. The trachea and the esophagus will be found to be encased in a common sheath, which is to be incised, exposing the esophagus in the posterior part of the wound and the trachea anteriorly. After this incision has been made the trachea and thyroid are then retracted toward the midline.

The esophagoscope is introduced by the esophagoscopist. The sac is emptied by aspiration, thereby avoiding expressing the contents into the larynx. The interior of the pouch and the lower pharynx are then painted with an antiseptic solution. The esophagoscope is then introduced into the fundus of the diverticulum and the sac transilluminated; then the esophagoscopist rotates the sac into the wound (Fig. 8, A). The sac is grasped with intestinal forceps and drawn upward and outward (Fig. 8, B). The esophagoscope is then withdrawn from the pouch. The sac is then freed to the junction of the diverticulum with the pharynx (Fig. 8, C). Care must be exercised to free all muscle fiber from its neck. The neck of even the largest diverticulum is seldom one-half inch in diameter. A neck larger than this usually means incomplete dissection. The sac is then transfixed at its junction with the pharynx with a small intestinal needle carrying No. 1 chromisized catgut in much the same manner as a hernial sac is transfixed (Fig. 8, D). The neck of the sac is severed close to the pharynx (Fig. 8, E). The stump is cauterized with pure phenol (Fig. 8, F). After transfixation, ligation, and amputation, the stump is invaginated with two mattress sutures of No. 1 chromisized catgut, one above and one below the stump (Fig. 8, G and H). These sutures penetrate only the submucous coat of the pharynx. This invaginated area is then covered by suturing together the cricopharyngeus and the inferior constrictor muscle. If the pouch originates at Killian's slit, the cricopharyngeus and the upper circular fibers of the esophagus are united (Fig. 8, I and J). Here, care must be exercised, not to include the inferior laryngeal nerve. During this procedure of muscle repair, the esophagoscope is in the esophagus. This detail is absolutely necessary in order to obviate stricture at the esophagopharyngeal junction. If this precaution be followed, none of the patients will require subsequent dilatation of the esophagus.

The incision in the neck is closed in layers, no drainage being used except a small piece of rubber tissue or cell-silk placed beneath the deep fascia.

RÉSUMÉ OF STATISTICS

Age	
Youngest	40 years
Oldest	75 years
Average	59 years
Sex	
Male	84%
Female	16%
Length of present illness	8 months to 40 years
Preliminary gastrostomy	8
Average time between operation and discharge	22 days
Type of operation	
1 stage	76
2 stage	3
Complications	
Acute dilatation of heart	2—(recovery)
Uremia	1—(death)
Pneumonia and atelectasis	1—(death)
Anesthesia	
Intratracheal	
Rectal	
Avertin	
Esophagoscopist	
Dr. Chevalier Jackson	12
Dr. Louis H. Clerf	67

SUMMARY

1. In a series of 76 pharyngeal diverticula, all operated on by the one stage method, there were 2 deaths.

2. Seventy-four patients had complete recovery.

3. None of the cases was complicated by mediastinitis.

4. None of the cases required postoperative esophageal dilatation.

5. The use of the esophagoscope prevents angulation, stenosis, and atresia of the esophagus.

6. Hoarseness is often a chief complaint.

7. There are 3 areas of the pharynx from which diverticula may arise.

8. The one stage method of operation is the reasonable method of treatment of pulsion diverticula of the pharynx.

9. The results depend upon rational surgical procedure and accurate approximation of tissues.

ADDITIONAL NOTES

Moynihan (Surg., Gynec. & Obst., Vol. 54, 1932) believes that there is no need for operations in two stages. He has operated upon 15 cases and has "never had any difficulty in obtaining healing by first intention."

Torek (Ann. Surg., Vol. 97, 1933) says: "Thirty years ago the mortality was very high with the one stage procedure, but in the last 5 years, 60 cases have been recorded with a mortality of only 1."

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DIVERTICULA IN THE ANTERIOR URETHRA IN MALE CHILDREN[1]

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DIVERTICULA of the urethra may occur in both males and females. In males the diverticulum may be located in the anterior or in the posterior urethra and it may be congenital or acquired. In general, it may be said that urethral diverticula are rare and in children especially rare. A brief survey of the literature reveals only 20 cases in which the diverticulum was located in the anterior urethra in male children.

Because the condition is so rarely found I wish to report the following case.

J. C., male, aged 6 months, was admitted to the Children's Memorial Hospital on February 18, 1934, on the service of Dr. C. A. Aldrich, to whom I am indebted for the privilege of reporting the case.

Dribbling with difficulty in passing urine had been noted since birth. For 2 days there had been intermittent attacks of crying, with fever for 2 hours and convulsions for 2½ hours.

The onset of the present acute illness began 48 hours before admission to the hospital, with attacks of crying, and an associated bulging in the upper end of the scrotum. The mother stated that the base of the penis had always been large, that the patient always had difficulty in passing his urine, that the urine came away in dribbling and that the child had to use considerable force to urinate. For about 24 hours no urine had been passed.

The child had had no previous illnesses. He was one of twins and his brother was normal.

Physical examination revealed an evidently acutely ill, pale child, grunting as if in severe pain. The head, neck, heart, and lungs were negative. The liver and spleen were palpable. A suprapubic tumor was found that extended ½ inch above the umbilicus, due to a full bladder. At the base of the penis was seen a swelling about the size of a crab-apple. Both testes were present in the scrotum.

An indwelling catheter was inserted into the bladder and the bladder was gradually emptied. The swelling at the base of the penis persisted.

Temperature on admission was 102 degrees. Examination of the urine (obtained from the indwelling catheter) showed: albumin, 3 plus; 50 to 100 white blood cells and 10 to 15 red blood cells per low power field. The phthalein test showed a total output of 42 per cent for 3 hours; blood chemistry showed non-protein nitrogen, 44. The blood count revealed white cells 25,000. The urethrogram (Fig. 1) disclosed a large round shadow in the urethra about the size of a quarter. A lateral roentgenogram showed a shadow about 1 inch long.

Pressure on the diverticulum caused the urine to run out of the external urethral orifice alongside the catheter. The diverticulum then diminished in size.

The pre-operative diagnosis was diverticulum of the urethra with complete retention of urine, acute cystitis, and acute pyelitis. Operation consisting of suprapubic cystostomy was advised.

At operation, February 22, 1934, a suprapubic cystostomy was done. Ether anesthesia was used. A No. 14 mushroom catheter was inserted and held in place by a chromic catgut suture. The bladder was closed with interrupted sutures of catgut.

Eight days after the operation the diverticulum became red, swollen and tense, and a pin-point opening developed on top of the diverticulum. A diagnosis of infection of the diverticulum was made.

A second operation was done March 3, 1934 (Fig. 2). Under ether anesthesia a pin-point opening in the scrotum was enlarged. Several ounces of thick, yellow pus were evacuated from the diverticulum which was then isolated by blunt dissection and amputated just above its entrance into the urethra. A soft rubber catheter was introduced into the bladder and the opening in the urethra was closed in two layers with catgut.

Instead of removing the sac at its attachment to the urethra, it was amputated directly above this point, the small fringe of the neck of the sac being utilized to close the defect in the urethra. The object of this procedure was to prevent the formation of a stricture of the urethra at this point.

The child made an uneventful recovery and was discharged from the hospital on April 10, 1934. Since leaving the hospital a stone has been passed. On chemical examination the stone showed a mixture of calcium phosphate, triple phosphate, and a trace of urate.

ETIOLOGY AND PATHOGENESIS

Many theories have been advanced to explain the origin of this condition. It may be interesting to present briefly some of these theories.

One of the early authors who attempted to explain the origin of diverticulum of the urethra was Voillemier (1868). In his opinion diverticula of the urethra are due to a lack of development of the spongy tissue of the urethra, the condition being similar in many respects to hypospadias, with the difference that in the latter condition the defect includes all tissues of the penis, including the skin.

According to DePaoli (1885) urethral diverticula are due to primary atrophy of the corpus spongiosum, allowing a bulging of the urethra to form a sac on the ventral wall.

Kaufmann (1886) advanced the theory that urethral diverticula result from urinary obstruction in fetal life; the obstruction being caused by a delay in the disappearance of the septum between the penile and glandular portions of the urethra. Thus a delayed union of the two portions of the urethra occurs, the urinary flow being obstructed, causing an expansion of the wall. The valve-like structures described by Hueter are persisting remnants of this septum. These valves are not interpreted as the cause of the diverticulum, but are interpreted as a contributory factor in the increase of its size when once developed.

[1]From the Children's Memorial Hospital, Chicago.

Fig. 1. Showing diverticulum of urethra. Note presence of catheter in urethra.

Petz, quoted by Bokay (1900), states that the diverticulum in his case was due to a congenital stricture of the urethra.

Watts (1906) expresses the following opinion as to the origin of urethral diverticula: "Since acquired true diverticula are usually the result of obstruction to urination, we should expect such an obstruction to be an important factor in the formation of urethral diverticula in early life. Such obstruction in childhood or intra-uterine life may be due to adhesions of the prepuce to external meatus, a congenital narrowing of the preputial orifice, or a congenital stricture of any portion of the urethra."

He then discusses the valve-like structures which occur in the urethra in certain cases and states that they may constitute a cause of obstruction. He notes that only in 2 of the cases which he studied (Hueter and Schlueter) could the formation of the diverticulum be ascribed to valves in the urethra. In these 2 cases, at operation, a circular valve was found at the outer extremity or diverticulum.

He adds that in the case of Hendriksz a valve-like structure was found which was apparently only a thickening of the urethral wall. Also, in some cases the valves mentioned as occurring at the anterior and posterior extremities of the diverticulum are merely secondary formations due to undermining of the urethral wall by the diverticulum as it increases in size. Bokay (1900) substantiates Watts' theory and states that the valves in one of his cases were formed in this manner. Watts has found that such valve-like structures are often present in acquired diverticula, resulting from perforation of the urethra.

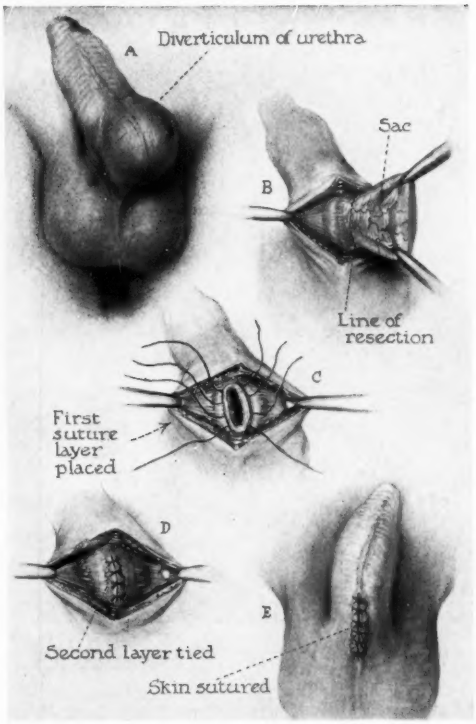

Fig. 2. *A*, The diverticulum. *B*, Isolation of the sac. Dotted line shows point of resection. *C*, First row of through-and-through sutures in place. The sac has been amputated just above the urethra. *D*, Second row of sutures. *E*, Suture of skin with fine silk.

A very interesting theory regarding the origin of urethral diverticula has been put forth by Suter (1908). He bases his theory on a histological study and concludes that diverticula of the urethra should be regarded as epidermal pockets communicating with the ventral wall of the urethra. He explains the embryology of the condition as follows: "The urethra originating from the genital furrow is covered with epidermis. A canal is formed which occupies the position of the future urethral canal. This canal is at first not closed on the side of the ventral surface of the future urethra, and there is a communicating bridge of epithelium connecting with the external skin. Normally this epithelial bridge (which remains squamous, while that within the canal becomes cylindrical) is absorbed." It is the persistence of this bridge which, according to Suter, gives the origin to diverticula and also to dermoids (Fig. 3).

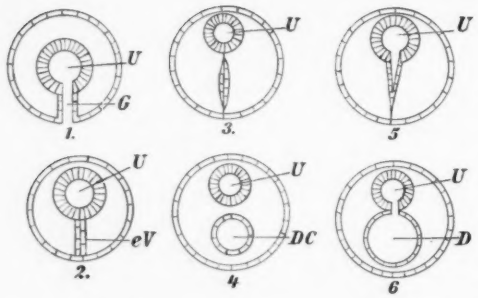

Fig. 3. From Suter. *1*, Showing the urethra, *U*, and the genital gutter, *G*. *2*, Genital gutter closed; bridge of epithelium, *eV*, remaining. *3*, Epithelial bridge disappearing. *4*, Cystic dilatation of the bridge giving rise to dermoids, *DC*. *5*, Incomplete closure of the epithelial bridge. *6*, Dilatation of the incompletely closed bridge of epithelium, gives rise to the diverticulum, *D*.

Cabezas (1913), after a review of the various theories of etiology, makes the following summary of his conclusions:

1. There is considerable probability that these dilatations result especially, as Durand affirms, from a disturbance in the development of the various tissue strata of the urethra, due to an abnormal blood supply, particularly in the spongy tissue.
2. In other cases, one may invoke not a disturbance but a defect in the development of these strata, the corpus spongiosum being totally wanting in the region of tumefaction. This can be explained only by an incomplete closure of the urogenital gutter.
3. The presence of a valve in a dilatation of the urethra is only to be considered as an adjuvant cause (joining its mechanical action with that of urinary pressure) in a defect already formed or on the way to formation.

AGE

A review of the literature reveals that 4 cases in which patients were less than 1 year of age have been reported (Busch, Bokay, Cabezas, Ternovsky); however, only 2 of these patients were operated upon. The case herein reported was 6 months of age, thus making it the third patient under 1 year of age who was operated upon.

It may be interesting to mention that in Lotzbeck's case the condition was diagnosed as late as the twenty-first year, although the symptoms had been present since early childhood.

The age incidence is given in the accompanying table.

LOCATION

Congenital diverticula of the anterior urethra occur on the ventral wall of the urethra. They are frequently located immediately behind the fossa navicularis and open with a narrower or wider mouth into the urethra.

Denk states that in 23 cases of congenital diverticula which he gathered in the literature (including his own case), 14 arose just behind the fossa navicularis, 7 were in the pars cavernosa (prebulbar), and 2 were in the pars bulbosa. Denk observes that the fact that the classical congenital diverticulum of the urethra is situated in the anterior portion is in accord with Kaufmann's theory as to their origin, namely, that they are due to a retarded establishment of communication between the penile and glandular portions of the urethra.

Drachter states that congenital diverticula of the urethra are for the most part in the pendulous and scrotal portions and on the under surface of the urethra.

SIZE

The diverticular pouches are described as varying in size from a hazelnut to a walnut or pigeon's egg. In the case of Hendriksz (quoted by Watts) the size of the diverticulum was stated as being greater than the capacity of the bladder.

CLASSIFICATION

Diverticula of the urethra may be classified as congenital and acquired. The congenital diverticula are seen in the anterior urethra and in a large percentage of cases occur in young subjects, or in patients whose history, suggesting a urethral diverticulum, dates back to early life. Movat says that when there is complete absence of any history of colic, thus precluding the possibility that a stone has descended to lodge in the urethra, and when there is no stricture or local lesion likely to give rise to a urethral or a para-urethral stone formation or other lesions to account for the origin, diverticula must be considered as congenital.

Likewise we must consider as congenital the cases arising in infants and also in children whose symptoms date to birth.

The acquired diverticula occur for the most part in the posterior urethra and the causes, such as urethral calculus, stricture, perforation of the urethra resulting from injuries or rupture of cysts, do not as a rule occur in childhood.

It has been suggested by early writers that the congenital and acquired varieties are to be differentiated by the fact that the former have a lining of mucous membrane similar in nature to, and continuous with, mucosa of the urethra, while the latter are devoid of a mucosa. It is generally admitted at this time that such a distinction is false, since inflammatory processes within a diverticulum may destroy the mucosa.

ASSOCIATED PATHOLOGY

The urethral diverticulum not infrequently becomes the site of an inflammatory process caused by the stagnation of the urine within it and by superimposed infection. This may lead to a fistulous opening on the surface of the penis.

Calculus formation may occur in a diverticulum and in the case reported by Grube in a child of 8½ years, the sac contained 162 small stones. Stones were present in Cabezas' case.

The obstruction to the flow of urine, caused by the pressure of the filled sac upon the urethral lumen, leads to dilatation, infection, and destruction of the upper urinary tract.

In the cases which have come to autopsy (Bokay, 2 cases, Ternovsky, Frontz), the effects of urinary stasis were evident in hydro-ureter, hydronephrosis, pyonephrosis, and pyelonephritis.

SYMPTOMS

In some of the cases the diverticulum could be emptied completely by pressure only to fill up again subsequently. In my case it was possible to empty the diverticulum completely by the introduction of a catheter into the diverticulum. Pressure upon the tumor in my case discharged purulent fluid (urine and pus) at the external meatus.

However, when diverticula become infected, certain changes occur in the tumor, namely, the skin becomes red and the diverticulum becomes attached to the skin; perforation of the skin with discharge of urine and pus soon occur. This train of events *occurred in my case.*

Although complete retention of urine is rare, this symptom was the direct cause of the patient's admission to the hospital in the case reported in this paper. The retention is mechanical in origin. The presence of the large diverticulum causes pressure upon the urethra, hence complete retention follows.

The outstanding clinical finding in this condition and one which occurred in every case which we have studied, is a tumor of the ventral surface of the penis. This tumor appeared in some cases during urination and in others is described as increasing in size during urination. In most cases it is noted that pressure on the tumor caused urine, or watery pus (in infected cases) to issue from the external meatus; and at the same time the tumor would diminish in size.

As a rule, the tumor is not attached to the skin and is generally described as being freely movable laterally; it is not tender on pressure nor are there external evidences of inflammation.

Disturbances of urination are encountered in the form of incontinence, or dribbling due to slow emptying of the pouch, difficulty, a small stream, or the passing of urine by drops. In the case of Laugier-Anger (cited by Watts after Guyon) the patient voided normally, but the pouch filled first and then the stream appeared.

In the cases of Hendriksz and Lotzbeck, Watts states that the urine was never voided in a stream. All the urine entered the pouch and was emptied by pressing the pouch with the fingers.

Nicholson states that in the absence of infection and urinary obstruction, it is quite possible for diverticula to be non-productive of symptoms. Especially is this true of smaller ones which readily empty and are thus free of stagnating urine.

DIAGNOSIS

As a rule the diagnosis of diverticulum of the anterior urethra is relatively easy. In my case the diagnosis was based upon the following:

1. The presence of a soft fluctuating tumor on the ventral surface of the penis.

2. Pressure upon the tumor was followed by a discharge of urine and pus at the external urethral orifice with a complete disappearance of the tumor.

3. Associated disturbances of urination, and finally complete retention of urine, necessitating the use of an indwelling catheter.

4. Diagnosis was verified by urethrogram (Fig. 1).

PROGNOSIS

The prognosis in these cases is entirely dependent upon the extent of the pathological changes which the diverticulum has caused in the upper urinary tract through obstruction and ensuing infection; and this means early diagnosis and early surgery before the onset of irreparable damage to the upper tract.

When the patient is operated upon before urinary stasis has caused serious damage to the upper urinary tract, the prognosis is good. This is seldom the case when the operation occurs after the urinary tract has been damaged.

TREATMENT

Excision of the diverticulum is the best form of treatment in this group of cases. Invagination of small diverticula may be tried; but as the majority of patients have large sacs, the invagination is not feasible. Moreover, invagination of a large sac may produce urethral obstruction. The relative ease and simplicity of diverticulectomy and the fact that excision removes the sac once and forever, justifies the statement that excision of the sac is the method of choice.

DIVERTICULA OF THE ANTERIOR URETHRA IN MALE CHILDREN

Author Date	Patient's age	Symptoms	Duration of symptoms	Method of diagnosis	Location	Treatment	Result	Remarks
1. Hendrikss (quoted by Watts) 1842	8 yrs.	Tumor on lower surface of penis, distended during urination. Pressure with fingers emptied the sac	Not stated	Inspection	Lower surface from fossa navicularis to penoscrotal junction	Excision of diverticulum and slitting of valve-like folds of mucosa found at anterior and posterior openings of urethra into the pouch	Good	
2. Lotzbeck (quoted by Watts) 1861	21 yrs.	Pouch at lower border of penis before urination. After urination pouch collapsed and penis was normal in appearance	Since early childhood	Inspection and introduction of catheters	Lower border of penis	Operation refused	Not stated	
3. Laugier-Anger (cited by Watts after Guyon) 1863	3 yrs.	Tumor on lower wall of urethra. Sound introduced along inferior wall caught in pouch	Since birth	Inspection and introduction of sounds	From fossa navicularis to middle of penile urethra	Excision of pouch 5 years later by Voillemier	Not stated	Pouch lined by mucous membrane. The corpus spongiosum absent. There were no valves at junction of pouch with urethra
4. Busch 1866	4 mos.	Pouch on under surface of penis	Since birth	Inspection and sounds	Under surface of penis	At 4 months diverticulum was incised and edges sutured to skin. Subsequent attempt to repair by Busch	Not stated	
5. Grube 1867	8½ yrs.	Swelling on under surface of penis at penoscrotal furrow	18 mos.	Inspection	Under surface at penoscrotal furrow	Removal of stones from bladder and from diverticulum. Diverticulum not excised but the edges of the urethral orifice were freshened and sutured	Healing	Diverticulum contained 162 small stones. Grube considered it congenital as a result of faulty closure of 2 valves of the urethral groove, causing a shallow cavity in floor of urethra in which a stone lodged, giving rise to urinary obstruction, new stone formation and progressive dilatation of the urethra
6. Hueter 1869	4 yrs.	Dribbling of urine. Tumor on under surface of penis	Since birth	Inspection and introduction of catheter into pouch	Under surface from fossa navicularis to scrotum	Excision of diverticulum and valve	Good	Dribbling was first attributed to paralysis of bladder. Another physician thought it was due to a narrowing of preputial orifice and incised the orifice. Hueter explained it as due to a valve-like closure of the urethra.
7. Schlueter (quoted by Watts) 1877	10 yrs.	Dribbling. Tumor on under surface of penis. Tumor collapsed when emptied with catheter	Not stated	Inspection	Fossa navicularis to scrotum	Excision of diverticulum and valve-like fold of mucous membrane which were at anterior extremity of diverticulum	Good	
8. De Paoli 1885	2½ yrs.	Swelling on under surface of penis. Reached size of hen's egg on urination	Not stated	Inspection	Under surface of penis	Partial excision	Not stated	Considered due to a weakness in urethral wall with dilatation; a result of primary atrophy of corpus spongiosum
9. Petz (quoted by Bokay) 1890	3 yrs.	Tumor of penis. Difficult urination. On catheterization, obstruction met at 3 to 4 cm. from meatus	1 year			Pouch opened and edges of orifice communicating with urethra freshened and sutured	Healing	Petz considered this case a congenital stricture of urethra which had caused dilatation of urethra and a diverticulum
10. Bokay Case 1 1890	3½ yrs.	Difficulty, dribbling, retention, swelling of penis on urination to form a tumor the size of pigeon's egg	3 weeks	Inspection and examination with catheter	Lower surface of urethra	Operation postponed due to poor condition. Irrigations of urethra and bladder. Constitutional treatment	Some cystitis and death after about 1 month	Autopsy showed evidences of obstruction and infection in bladder, kidneys, and ureter. On lower wall of urethra 4 cm. from external meatus was an oval opening 6 x 14 mm., leading to diverticulum (size of plum) and to mucosa whica was continuous with that of urethra

DIVERTICULA OF THE ANTERIOR URETHRA IN MALE CHILDREN—Continued

Author Date	Patient's age	Symptoms	Duration of symptoms	Method of diagnosis	Location	Treatment	Result	Remarks
11. Bokay Case 2 1890	3 wks.	Difficult urination. Continual dribbling. Soft fluctuating tumor on under surface of penis. Pressure on tumor caused flow of urine at meatus	Since birth	Inspection and catheterization	Lower floor of urethra near fossa navicularis	Operation for phimosis Operation for diverticulum refused	3months later, death seemed imminent	
12. Bokay Case 3 1890	3 yrs.	Dribbling, frequent painful urination, pyuria. Tumor size of hazelnut on lower portion of penis near penoscrotal junction; became size pigeon's egg on urination and emptied on pressure of fingers	1½ yrs.		Middle of pars cavernosa urethra	Excision	Death after 2 months	Autopsy showed dilatation of kidneys and ureters
13. Durand (quoted by Watts) 1901	2 yrs.	Tumor on under surface of penile urethra	Not stated	Objective findings	Communicated with urethra by an orifice 1 cm. in length 1 cm. from external meatus	Excision	Not stated	All coats of urethra including spongiosum were represented in wall of pouch
14. Escat 1908	5 yrs.	Fluctuant tumor of lower border of penis	Not stated	Not stated	Penile urethra on ventral surface	Extirpation	Recovery	
15. Haberean 1911	8 yrs.	Tumor on under surface of penis; increased in size during urination. Slow, small urinary stream	Not stated	Objective findings	Lower surface of urethra, from behind fossa navicularis to middle of pendulous urethra	Excision	Good	
16. Denk 1912	8 yrs.	During urination a balloon formed on under surface of penis. It emptied by slow dribbling after act of urination was completed	Noted soon after birth	History and objective findings	Began behind glans and involved two-thirds length of penis	Extirpation	Excellent	
17. Cabezas Case 1 1913	In 1st yr.	Tumor on under surface of penis during urination. Did not empty completely and urine could always be expressed from it	Since birth	Objective findings	Ventral surface of penile urethra	1. Artificial hypospadias 2. Resection of diverticulum 4 years later	Good	Resection not done when first seen due to poor general condition. Seen first under 1 year of age. Operated at 5 yrs.
18. Cabezas Case 2 1913	14½ yrs.	Recurring attacks of retention. Tumor of penis, size of walnut	Since 4 yrs. of age		Cavernous urethra	Excision	Not stated	Diverticulum contained a large number of small calculi
19. Ternovsky 1930	10 days	Tumor at root of penis. Pressure on it caused urine to exude at external meatus. Disappeared when catheterized and returned an hour later	Since birth	Inspection and palpation. Verified by urethrogram	Under surface of penis at border of scrotum	No operation	Death	Autopsy findings: Hypertrophy of bladder wall, cystitis, hydroureters, pyelonephritis and pyelonephrosis
20 Frontz 1931	14 mos.	Soon after birth, urinary obstruction. Tumor visible beneath scrotal skin. Pressure on this gave escape of watery pus at external meatus, and collapse of tumor	Noted soon after birth	Autopsy	Diverticular orifice (2 cm. in diameter) on inferior wall of mid-bulbous urethra	No surgery attempted	Death from uremia a week later	Autopsy findings: Valve-like fold at the entrance of the diverticulum which allowed urine to distend the sac but prevented its emptying. When the sac was distended the bulbous urethra was compressed from below upward. Extreme hydroureter, hydronephrosis and pyonephrosis
21. Kretschmer 1935	6 mos.	Difficult urination. Swelling on under surface of penis. Complete retention	Since birth	Inspection and palpation Aspiration with catheter Urethrogram	On left side of penoscrotal junction	Diverticulectomy	Cure	

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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1905–1935

ALLEN B. KANAVEL, M.D.....Editor
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MARCH, 1936

CANCER AND PUBLICITY

PUBLICITY in the fight against cancer acts as a two-edged sword. It points the way to the prevention and to the early treatment of cancer in all its forms. It stimulates the hope that the public may be made conscious of bodily abnormalities or irregularities which should be investigated. It provides the opportunity for physicians to inform the people of the known and tested methods by which these diseases may be combated. If the agencies which supply such publicity would stick to "fighting cancer with facts," the good which they could accomplish would be immeasurable. There is a painful tendency, however, not only to supply the facts, but also to pass on as facts, the new untested fancies because of a quality they possess which is known as "news value."

It is this unfortunate feature of the publicity in dealing with the cancer problem to which we should give particular attention. The news agencies, which are the worst offenders, seem to get especial satisfaction in ferreting out, old, discarded forms of treatment. These are dressed up as great unheralded discoveries and fed to the long suffering public. Thus, within the last 6 months one of our smart weekly magazines has given artificial respiration to at least three prostrate "cancer cures." It has propped them up and supported them with its rhetoric, at the same time making witty, slurring remarks about the organized medical profession which saw fit to reject these discoveries. The news agencies will frankly admit that they are interested in gathering and publishing anything that is news. They will point out that the public interest in cancer has been aroused and that cancer stories make good headline features. People are anxious to hear about work in this field. If it is explained to news men that the cancer problem is one of great difficulty; that scientific men have spent their whole lives on single special parts of the problem; that great institutes have been established throughout the world where coordinated organized research is being conducted by expert specially trained investigators; that cancer comprises a large group of different diseases with as great differences between them as typhoid fever is different from measles; that, even in regard to the infectious diseases, nobody is foolish enough to look for one "single cure" for all of these infections at the same time; even if the problem is made as clear to the news agencies as it can be stated, there will still appear the alluring headline—"Backwoods doctor discovers cure for cancer." This hardy plant, though not an an-

nual, appears at least as a biennial. It is too much to expect that the news men will confine their attention only to "all the news that's fit to print." It is too often apparent that fitness as such does not enter. The great need of the news agencies at the present time is the development of a desire for accuracy and for a conscience. These apparently harmless headlines are usually the cause for the movement of a caravan of helpless sufferers toward a forlorn hope. They go at no matter what sacrifice, regardless of the distance. They pour out their life savings expecting the miracle which the papers have promised. The mass psychology buoys them up for a time. Then, failure and despair. The excitement over, the newspapers turn to other more sensational items. The failure, which would also seem to have "news value" somehow never gets mention. The papers sometime could at least tell us where are the cures of yesterday which crowded all these poor people about the shrine of the discoverer.

The whole fault with this unwholesome cancer publicity is not entirely with the news agencies. The scientific investigators must also share a part of the blame. Any scientist who is conducting studies on any phase of the cancer problem should be unusually careful in what he publishes. The very anxiety of the news reporters will frequently cause them to misinterpret or to exaggerate the claims of the scientist. Scientific reports should clearly state that the experiments so far have been carried out only on animals. If the results seem to warrant a trial in human cancer, it should be easy to get some of the reputable medical schools or cancer research institutes to co-operate. This would in no way detract from the credit of the investigator. It would only tend to prove that the scientist had an honest belief in his remedy. It would indicate that he wished corroboration from unbiased observers. This is the way that insulin was introduced to the medical profession by Dr. Banting. He did not insist that his remedy be kept secret. He did not start a procession of diabetics to Toronto. He quietly asked several of the leading medical school clinics to try out his agent against diabetes. This did not take any of the glory from the greatness of his discovery. It simply proved quickly that he was right. The same would be true in regard to any proposed treatment for cancer. When the scientific investigator gives an interview to the press before his discovery has been reported through regular medical channels, it lays him open to criticism on at least two counts. It shows a disregard for the other members of his profession who by right should know of new developments in medicine before the general public does. It is only fair that physicians who will be called upon to advise their patients should have a chance to think about the new treatment. It furthermore shows a naive simplicity on the part of the discoverer who thinks he can make such an announcement and escape the consequences. It makes the more cynical members of society look upon it as a desire to meet the consequences at any price,—provided it is high enough. The cancer research worker must be patient, painstaking, and deliberate. He must possess balanced judgment. He must subject his results to critical analysis. He must not let his enthusiasms bias his opinion. He must make his mind control his emotions. He must not jump to conclusions before he has tested and retested his results. When it is recalled how many apparently sane investigators have gone wrong on the cancer problem, it is evident that this field is full of pitfalls. Even the head men of cancer institutes have made mistakes in backing and promoting some of the seeming discov-

eries of their staff. The fault in such instances is in assuming more than the results have warranted. The repeated disappointments in cancer cures naturally have made authorities in this field very skeptical about new discoveries. They wish an opportunity to try them out before accepting them at face value. This is in a way unfortunate. It perhaps may make a slower acceptance of some fundamental discovery which may unlock the doors to progress. It also makes the tyro believe that these men are prejudiced against any new line of investigation. He consequently develops a martyr complex, which unhappily is fostered by the many agencies. The embryo scientist is pictured as a St. George fighting against the dragons of organized medicine.

In reality, the cancer authorities are simply trying to protect the public against exploitation. The appeal made by the new discovery attracts a large proportion of the public. The mass of the people accept it because of its emotional appeal; the intellectuals, because they are constantly on the alert for the new. The latter group are often more deceived than the former. They lack the proper background to make a reasonable estimate. The public, consequently, is also partly to blame for the uncontrolled publicity given to the cancer problem. If the public would react in some sensible way to these announcements instead of accepting them as reported, progress would be made. If the public would demand that the news agencies back their statements by the endorsement of recognized authorities in the field; or that the news of medical items should be handled through a publicity committee of the county medical society; if it could be made uncomfortable for those who broadcast false information; or if all the people would refuse "to be fooled all the time" by the papers but would receive their misinformation with jeers and ridicule, — there might be a more honest attempt to get information of value rather than for its sensational qualities. The news of cancer would not in itself have malignant qualities as it does now when "it serves no useful purpose."

JOHN J. MORTON.

APPLICATION OF FIXED TRACTION FOR TRANSPORTATION OF PATIENTS WITH FRACTURES

THE United States census reports show that there were 36,000 fatalities from automobile accidents in 1935. It is estimated from reliable figures that there occurred one million fractures during this period from the same cause.

Sir Anthony Bowlby, head of the medical department of the British Expeditionary Forces during the early part of the World War, estimated that the mortality from compound fractures after the adoption of fixed traction in transportation was reduced from 80 per cent to 20 per cent. The stretcher bearer and the doughboy were trained to apply fixed traction on the battle field. It is now more than 17 years since the World War and we are not giving our ever increasing number of sufferers from high speed locomotion the same chance of life and health that was given our soldiers. During that time many more Americans have been injured or accidentally killed than in all the wars in which the United States has engaged.

It has been argued that the layman should not be taught to apply a splint for aid in transportation because of the implied entrance of the laity into the medical field. Nevertheless, no one would argue that a layman should not attempt artificial respiration in a case of submersion, or that a layman should not apply a tourniquet to prevent death from hemorrhage, provided a doctor were not available. Doctors are rarely present at the time

of an automobile accident. If, by the application of a Keller-Blake splint to the lower extremity or a Murray-Jones splint to the upper extremity, jackknifing of the fractured bones with resultant shock and delayed union can be prevented and the patient transported in safety to the nearest doctor or hospital for treatment, a great step in advance will be made.

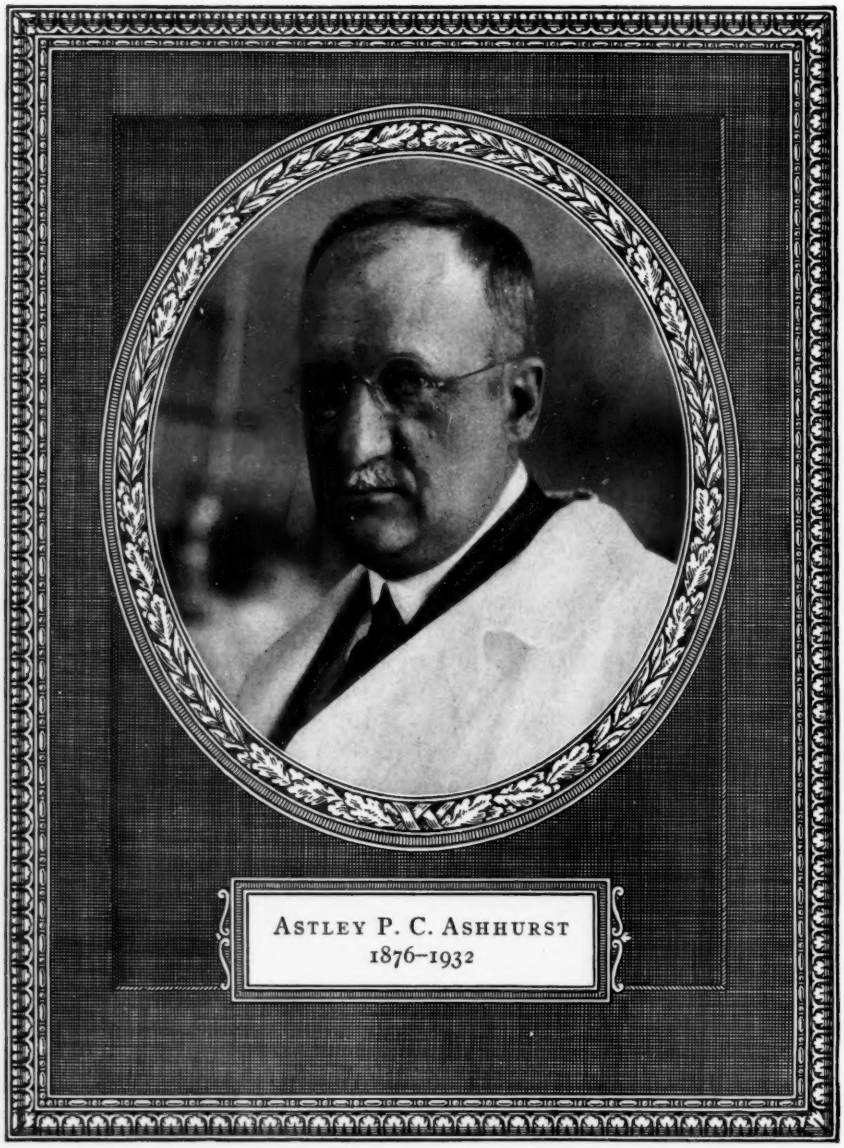
By medical and lay propaganda in many cities and states, the Committee on Fractures of the American College of Surgeons, through its regional groups, has stimulated interest in the safe transportation of fractures, and definite improvement is noted in many localities. Ambulances in general are manned by doctors, fire or police departments, or morticians, according to the section of the country. Instruction is being given to these various groups and many ambulances are now equipped with traction splints, but unfortunately only a comparatively small proportion of them has been reached.

The American Red Cross has been interested for a long time in the problem of emergency first aid along automobile highways. Instruction in the application of the Keller-Blake half ring splint for fractures of the lower extremity has been incorporated in the latest edition of its book on first aid. It is now establishing emergency first aid stations along many of the main highways. Traction splints are a requirement in the equipment of these stations, and their attendants are being trained in the application of immediate traction. The Committee on Fractures of the American College of Surgeons is co-operating with the American Red Cross by asking the members of its Regional Fracture Committees to assist in the necessary instruction to be given the attendants. There are at present 238 stations fully equipped and operating, and 1,440 are promised to be opened within the next 6 months. These stations are being started in 34 states.

The officials of the Boy Scout organization have taken up very actively the problem of transportation of the injured and, in all the camps throughout the country, the Boy Scouts are being trained in the application of fixed traction. The leaders of the Girl Scouts have indicated their willingness that similar instruction be furnished the girls.

The American College of Surgeons, having entered into this move to protect the traveling public, has assumed certain obligations. With the large amount of lay propaganda that is being disseminated by the American Red Cross, the Boy Scouts and the Girl Scouts, it is necessary that surgeons throughout the country should be themselves thoroughly informed of the method of applying fixed traction and should be willing to offer their services to aid these organizations should they be so requested. If these requests come from the American Red Cross, it is advisable to follow the method described in the Red Cross book on first aid. There can be no question that if transportation of patients suffering from fractures can be so improved injury incurred during transportation will not be added to the original injury, the saving of life, and the decrease in the period of hospitalization will be of great economic benefit to mankind.

FREDERIC W. BANCROFT.
Chairman, Committee on Fractures
American College of Surgeons



ASTLEY P. C. ASHHURST
1876–1932

UNIV. OF MICH.

MASTER SURGEONS OF AMERICA

ASTLEY PASTON COOPER ASHHURST

FROM Colonial days Philadelphia has contributed more than its share to the progress of medicine. Soon after the middle of the eighteenth century a group of young Americans returned from Edinburgh imbued with the spirit of that school. It was not long before Morgan and Shippen started the first medical school in Philadelphia, and were soon joined by Kuhn and Rush. Since that time there has been a steady stream of men whose writings and teachings have spread throughout the land the results of their own searchings after truth. Bond and Barton, Wistar and Physick, the Hares and Woods, the Hodges and Penroses, Agnew and Leidy, the Peppers and Ashhursts.

Astley Ashhurst early appreciated the responsibilities he had inherited from his father, John Ashhurst, Jr., professor of surgery at the school Morgan had started. His devotion to this profession and its ideals was the dominating influence in his whole life. Except for his war service, his entire career was spent in Philadelphia. He was born there August 21, 1876, his mother being Sarah Stokes Wayne Ashhurst. He prepared at the Forsyth School, now the Episcopal Academy, a private college preparatory school located in Philadelphia, and entered the University of Pennsylvania from there, receiving his degree of Bachelor of Arts in 1896 and his Doctor of Medicine in 1900. His classmates always remembered him as taking prizes in Latin and Greek and in taking senior honors in the Academic Department, and he was elected to membership in the Philomathean Society, the Phi Beta Kappa and the Sigma Xi fraternities, and graduated the first man in the senior class of the medical school.

After leaving the medical school he served an interneship from 1900 to 1901 at the Children's Hospital, and from 1901 to 1904 at the Episcopal Hospital. Following his interneships he served an apprenticeship in the dispensaries of the Episcopal, Orthopedic, Children's, German (now Lankenau), and the Pennsylvania Hospitals until 1913, when he was elected surgeon to the Orthopedic Department and associate surgeon to the Surgical Department of the Episcopal Hospital. In 1914 he was appointed surgeon to the Orthopedic Hospital and in 1915 he was promoted to the position of surgeon at the Episcopal Hospital. His training as prosector to Dr. G. G. Davis, professor of applied anatomy at the Medical School of the University of Pennsylvania, gave him a knowledge of

surgical anatomy which not only influenced his operative work, but hallmarked all his contributions to surgical literature. For 19 years, 1911 to 1930, he was an instructor in surgery at the University of Pennsylvania teaching operative surgery on the cadaver. From 1930 until his resignation in May, 1932, he was professor of clinical surgery at his Alma Mater.

From the establishment of teaching in the University's Graduate School of Medicine, in 1918, Dr. Ashhurst evinced great interest in the ideas and work of the School. In 1920 he became an associate in surgery in the School, in 1921 an associate professor of surgery, and in 1923 a professor of clinical surgery. The latter post he retained until his death, in 1932—although inactive from illness toward the end. His teaching of clinical surgery, to the graduate students of surgery, especially in the Episcopal Hospital of Philadelphia, exemplified those qualities of conscientiousness, erudition, and technical perfection which were his admirable characteristics.

His wide knowledge of surgical literature and his mastery of the fundamentals of surgery, together with his interest in teaching, made his lectures and quizzes popular with the students. The student's first impression of him was usually unfavorable. His hesitating speech, which was the result of stuttering in early manhood, together with his hypercritical respect for the truth were causes of his being at first misunderstood, but his sterling character and the justice of his criticism, not only of others but of himself, were soon appreciated by the students, and explains his popularity with them.

"As a surgeon he was methodical in the superlative degree," says Dr. Crossan, one of his associates, "and insisted upon performing every detail of the operation himself, including the application of the bandages. Neither brilliancy nor speed in operating was attempted by him and he seemed to abhor the spectacular. He was just as meticulous of the pre-operative and postoperative care of his patients as in his operative technique, and he would never accept the opinion of any one without himself consulting the evidence, making his own physical examination, examining the X-ray films and studying the gross microscopical preparation of the tissues."

He was proud of being a general surgeon and with such wide and varied training as he had received he was well fitted for such a broad field. Though tempted, after the death of Dr. G. G. Davis, to limit himself to orthopedic surgery, for which he had such an unusual training, he said that surgery of the bones and joints belonged to the general surgeon and that such a special field was too small to occupy the full time of a well trained surgeon. He was trained also in gynecology. For several years he did the neurosurgery at the Orthopedic Hospital.

Outside of Philadelphia, as one would expect, he was probably best known as an author. His scientific articles were not only clear and simple but uniformly accurate, and all of his contributions to surgical literature reflect his scholarly

attainments. As one would expect from his clinical work, he never accepted the statements of others in literature, but always ran them down to their source and frequently embarrassed his colleagues by his discovery of inaccuracies. One wonders where he found time for all this work, for between the years 1902 and 1920 he wrote 82 magazine articles, was co-author in 10 others, wrote numerous book reviews, edited 2 volumes of the Episcopal Hospital Reports, was a co-author of 2 textbooks (*Enlargement of the Prostate*, with Dr. John B. Deaver, and *Surgery of the Upper Abdomen*, with Dr. John B. Deaver) and published the first edition of his book *Surgery; Principles and Practice*, and the "Gross Prize" essay "An Anatomical and Surgical Study of Fractures of the Lower End of the Humerus."

He was a very active member of the Philadelphia Academy of Surgery and was rarely absent from its meetings. His presence was not passive in any sense, but always active up to the time of his illness. This activity consisted not only in his own presentations, but in a critical discussion of nearly every paper. He felt it the duty of every Fellow to prepare a discussion of the subjects presented at the meeting. His knowledge of the literature and careful preparation of his discussions stirred his fellow members to efforts usually beyond their inclinations. They all knew that he would be at the meeting and that he would make as great if not greater preparations for his discussion than they had in their presentation. His value to the Philadelphia Academy of Surgery cannot be overestimated. He delivered the annual address in 1910 and served as president in 1928 and 1929, and received the Samuel D. Gross Prize in 1910 for "An Anatomical Study of Fractures of the Lower End of the Humerus."

He was vitally interested in the College of Physicians and could be found in the building at some time during each day reviewing literature or discharging his duties as honorary librarian, a position he held from January 9, 1928, to the time of his death.

He was elected a Fellow of the American Surgical Association in 1913, and he brought to that association the same unique qualities which he exhibited in the Philadelphia Academy of Surgery. Astley P. C. Ashhurst could not be other than Astley P. C. Ashhurst—whether it was in Philadelphia, in the American Surgical Association, the Interurban Surgical Society, the Society of Clinical Surgery, the Society of Military Surgeons, the International Society of Surgeons, Association de Française de Chirurgie, the Academy of Natural Sciences, or the Historical Society of Pennsylvania, he was the same sterling scholarly character in search of medical truth.

His sense of duty and his belief in the obligation of service sent him to the first Officers' Training Camp organized at Plattsburg, in 1916. With America's entry into the World War he organized the Episcopal Hospital Base Unit 34 and was its first medical director. He was sent to France with this Unit December 15, 1917, and returned to America in 1919. In France he served at the front with

the French and the Americans, and after the Armistice was appointed as a consultant to the Hospital Center at Savenay. Upon returning home he was appointed chief of the surgical service at the Walter Reed Hospital, where he served until the time of his discharge from the Army, April 16, 1919. He entered the Army as a first lieutenant and was discharged as a colonel. He received a citation for "exceptionally meritorious and conspicuous service with Base Hospital 34."

"As a man he was almost a crusader for honesty and truth." With Ashhurst there was not such thing as a white lie or a gray lie. Truth permitted of no comparison and it was either a truth or a falsehood. Few of us have not winced at his criticisms and book reviews, which were rarely sought by writers or publishers because he insisted on recording what he believed to be true. His probity won him great respect even though it did not make him popular. His was a life devoted to surgery. He had no hobbies and his relaxation was study. Eventually the long hours of clinical work and study began to show their effects. In 1929, at the early age of 52, he began to suffer from dizzy spells and in the latter part of May, 1930, while driving his car on the Roosevelt Boulevard he had his first attack of cerebral thrombosis and crashed into a tree. He was able, however, after getting out of the wreck, to take a picture of it and make his way to his office by trolley and bus. Several hours after he reached home it was noticed that he had a left hemiplegia. After months of rest he entirely recovered the use of his hand and leg and gradually returned to operating and teaching. However, in the latter part of August, 1932, he had a second attack of thrombosis, from which he rallied, but a third attack on September 16, 1932, resulted in his death 3 days later. To those who knew him intimately he never made the slightest complaint or lament of his misfortune. When asked if he did not know that he was carrying high blood pressure, he replied, "Yes, but what is there to do about it?"

On July 16, 1930, he married Anna Campbell, during his remaining days his constant companion and devoted attendant. His wife and daughter survive him.

Ashhurst was not an ordinary man. He was rather tall but stooped shouldered, strong but gentle, never hurried but constantly active, apparently slow but accomplishing much, seemingly a crabbed bachelor but with a warm heart and understanding sympathy, a caustic but fair critic, dogmatic but open minded, not widely popular but much beloved, a diligent student all his days and a teacher of sound surgery. For over 30 years he met his inherited responsibilities and carried on the Philadelphia tradition. He contributed much and will be sorely missed by his patients, his students, and his friends. WALTER ESTELL LEE.

WILLIAM DARRACH.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

As a result no doubt of the disordered political and economic conditions throughout the world, there has been a dearth of original and enlightening radiological contributions in the field of diagnosis.

As in the former volumes of the *Year Book of Radiology*,[1] the authors again present concise, yet adequate reviews of articles which have appeared in medical literature during the preceding year. The material has not been selected from the radiological journals alone, but from the many periodicals covering the field of medicine and surgery. Many articles which appeared in European literature have been used. Barring the inversion of two or three, the 454 illustrations are well reproduced.

The first 303 pages of the volume are devoted to the field of radiological diagnosis. Although there have been no spectacular new developments, the articles have a quality which points to a high and efficient plane of diagnosis. Arteriography has become a helpful diagnostic procedure. More accurate roentgenographic study of the petrous bone has proved to be very valuable.

Economic conditions have interfered considerably in the field of cancer research and investigation. While no startling new results have been reported, the work in the United States has been carried on with renewed vigor. The field of radiotherapeutics covers 195 pages of the volume. Included in this section is not only material on radiotherapeutics, but numerous articles on other phases of the cancer problem such as etiology. Although there is a definite tendency toward increased voltage, its value has not yet been answered by experience. The same statement may be made concerning the efficacy of a big radium pack rather than the smaller unit. The protracted method of treatment along the lines advocated by Coutard has definitely proved its value, particularly in carcinoma of the upper respiratory tract. The value of radiation in the treatment of various benign conditions, such as infections, is gaining much favor.

The radiologist will find the volume very valuable as a handy source of reference. The satisfactory manner of presenting the material is commended and the volume is recommended to the busy physician not able to read the vast amount of material covered.

The 1935 volume[2] provides the radiologist with a handy source of reference to the important radiologic literature of the year. The volume is larger and contains more illustrations than the 1934 review. All phases of radiology, both diagnostic and therapeutic, have been covered. As in former volumes, the short, concise editorial comments concerning the articles which are abstracted enhance their value.

Part I, covering 338 pages, is devoted to the field of radiological diagnosis. Recent work in the roentgen study of the nervous system has been rather extensively abstracted. The value of thorotrast in the diagnosis of inflammatory foci in bones is of interest. Technical procedures such as "polisography," tomography, and kymography are gaining more attention. Other works of interest include various methods of localization of foreign bodies in the eye, breast radiography, serial bronchography, more accurate small intestine studies demonstrating inflammatory lesions and Meckel's diverticulum, refinements in cholecystography, diagnosis of placenta prævia by cystographic studies, pelvimetry and cephalometry and the non-surgical reduction of intussusception under fluoroscopic control. Especially timely, and of great interest to the radiologist, is the increasing tendency of widespread practice of medicine on the part of the hospitals. Articles dealing with industrial hazards, the medicolegal aspects of silicosis, and the economic problems of radiology are pertinent.

The field of radiotherapeutics is covered in Part II, consisting of 237 pages. The death rate due to cancer is increasing. Research work on the causative factors of cancer has been carried on with interest. Surgery and irradiation remain the most effective weapons at our disposal for combating the disease.

Advancements have consisted of attempts toward perfection of irradiation methods based on more extensive experience. The question of whether super X-rays are superior to those generated by the 200 kilovolt apparatus or the large radium pack, has not been settled. The various safe-acting safeguards of X-ray apparatus has been an important development. The shift to radiation rather than surgery in the treatment of cancer of the cervix has been an important advance. Recent work on the treatment of cancer cases with cobra venom showed it to be ineffective and to have no value in relieving pain. Radiation has gained increasing favor in the field of

[1] THE 1934 YEAR BOOK OF RADIOLOGY. Diagnosis. Edited by Charles A. Waters, M.D., Therapeutics. Edited by Ira I. Kaplan, B.Sc., M.D. Chicago: The Year Book Publishers, Inc., 1934.

[2] THE 1935 YEAR BOOK OF RADIOLOGY. Diagnosis. Edited by Charles A. Waters, M.D. Associate editor: Whitmer B. Firor, M.D. Therapeutics. Edited by Ira I. Kaplan, B.Sc., M.D. Chicago: The Year Book Publishers, Inc., 1935.

benign conditions. It has proved to be of real value in the various inflammatory conditions as well as in cases of endocrine disturbances.

The volume should not only be a valuable addition to the library of the radiologist, but to the busy physician or surgeon who does not have time to read the vast amount of material covered.

EARL E. BARTH.

ANOTHER Oxford medical monograph[1] embraces in 170 pages a careful review of the literature and a correlation of the now accepted facts. The reference material is worthy of especial comment. The chapter on physiological and pathological considerations is indeed worthy of note. The indications and methods for administering oxygen by different routes in different diseases has been considered on an obviously unbiased basis. Illustrations and clinical problems showing defects as well as success round out the material so as to render it very useful to the general practitioner.

The manner and methods compare favorably with those in use in America. American references and equipment play a prominent rôle in this volume. The authors are enthusiastic for the proper use of oxygen as are all who are familiar with its clinical application. They offer a hope for the early general adoption of an "oxygen service" which may be conducted on a voluntary basis and available to all alike. An excellent book bringing up to date the known facts relative to oxygen and carbon dioxide therapy.

M. HERBERT BARKER.

THE book[2] entitled *Apparatus and Technique for Roentgenography of the Chest* by Weyl and Warren, is a highly technical work comprising material dealing with the physical phenomena underlying roentgenography in general; the available roentgenographic equipment and its limitations; the practical application of such equipment for chest roentgenography; and methods of measurement and standardization of roentgenographic apparatus and technique. The authenticity of the work is attested not only by the institution from which it emanates, but also by the stamp of approval given by such men as Dr. Maurice McPhedran and Drs. Chamberlain and Pancoast.

There are doubtless numerous physicians who have become the possessors of roentgenological equipment whose major qualification for operating the apparatus consists in their possession of it. These physicians usually leave the actual technical operation of their equipment to technical assistants whose training has usually been skimpy and all too brief and their preliminary groundwork so lacking in mathematical and physical instruction they would find the mastery of this work rather tough going. Most radiological specialists are quite familiar with these principles and practice them in their current medical activities. Other physicians who essay the roentgenological examination of the chest would do well to study this excellent manual.

JAMES T. CASE.

IN a small book[3] of approximately 170 pages divided into ten chapters and an appendix, Tucker discusses injuries and their treatment. The appendix is devoted to the illustration of apparatus for the application of diathermy and radiant heat.

Judging from the preface and from the type of illustration used throughout the book, one concludes that the book is written principally from an experience based on athletic injuries. Soft tissue (muscle, tendon, ligament) injuries are dealt with for the most part, and bone, nerve, and visceral injuries are mentioned only in passing. In this regard the title is somewhat misleading. The book can hardly be regarded as a thorough work because so many subjects are touched upon in such a limited number of pages.

In general it would seem that the book would be more valuable in the library of an athletic trainer or a physiotherapist than in that of a surgeon.

JAMES K. STACK.

OUR ideas pertaining to tuberculosis and particularly as regards its treatment have been in such a stage of flux during the past 10 years that a work on this subject at this time compiled from the experience of thirty-four specialists in its various phases comes to the medical profession at an opportune time.

Clinical Tuberculosis[4] is much more comprehensive than its title would infer. The two volumes contain 48 chapters and in each of these the disease is attacked from a different aspect, with ample bibliographies at the end of each chapter. Epidemiology, pathology, physiology, classification, physical diagnosis, X-ray interpretation, symptomatology, medical treatment, surgical collapse, extrapulmonary tuberculosis, complications, etc., are covered in excellent detail. One might be carried away by the enthusiasm of Coryllos in his policy of delay while acclaiming the virtue of surgical apical collapse. There are still not a few who might question his early policy of waiting and not applying more simple surgical procedures while endeavoring to ascertain the character of the disease. His ideas are rather at variance with recent teaching which stresses early diagnosis and the prompt employment of less formidable procedures.

On the other hand, Hedblom leaves us a well

[1] OXYGEN AND CARBON DIOXIDE THERAPY. By Argyll Campbell, M.D., D.Sc. (Edin.), and E. P. Poulton, M.A., D.M. (Oxon.), F.R.C.P. (Lond.). Foreword by Sir Leonard Hill, F.R.S. London: Oxford University Press, 1934.

[2] APPARATUS AND TECHNIQUE FOR ROENTGENOGRAPHY OF THE CHEST. By Charles Weyl and S. Reid Warren, Jr. Moore School of Electrical Engineering, University of Pennsylvania. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1935.

[3] INJURIES AND THEIR TREATMENT. By W. Eldon Tucker, M.A., B.Ch. (Cantab.), F.R.C.S. (Eng.). New York: Oxford University Press, 1935.

[4] CLINICAL TUBERCULOSIS. Edited by Benjamin Goldberg, M.D., F.A.C.P., F.A.P.H.A. Vols. 1 and 2. Philadelphia: F. A. Davis Co., 1935.

balanced surgical viewpoint with due recognition of the value of phrenic surgery and pneumothorax.

There is necessarily much repetition and also contradiction in not a few instances. The latter is rather an asset for it presents the views of more than one author and leaves questions open for discussion. One cannot help but be impressed by the practical application of the writings of these thirty-four collaborators. It is perfectly evident that they are thoroughly familiar with the everyday problems presented to medical men specializing in this field of medicine.

The two volumes are well illustrated with over 640 halftone and line drawings and 9 full-page color plates.

While there is much that is superfluous and some unevenness in the quality of the work, still the chapters are all uniformly good and one can absorb useful bits of information from each and every chapter. The work is well organized and complete and correlates our knowledge of tuberculosis up to the present moment. These two volumes should be of interest to all students of medicine but particularly will they be of value to those specializing in tuberculosis.

The editor and his contributors should be highly complimented on their excellent and very thorough presentation and their work should take a high place in our literature dealing with tuberculosis.

JOHN W. TOWEY.

A GREATLY neglected subject has been excellently dealt with by Jameson in his monograph *Gynecological and Obstetrical Tuberculosis*.[1] Written as it is, by one who is well qualified both from the viewpoint of the phthisiologist and the gynecologist it fills a definite void in modern gynecological literature. The author has gathered together the complete literature on the subject and, in addition, has added his own studies, which were carried out at Saranac Lake, as well as his experiences in the autopsy room and at the bedside in the various sanatoria of this region. This material he has correlated from all of the various angles of the subject into a most comprehensive and readable work. For the first time, the modern knowledge of the physiology, diagnosis, and treatment of tuberculosis of the pelvic organs and the ever present problem of tuberculosis and pregnancy are adequately handled in one monograph. The book is most highly recommended.

RALPH A. REIS.

IN *The Principles and Practice of Surgical Nursing*[2] an effort is made by the author to present the nurse with a working knowledge of the diseases that the surgeon meets most frequently. It is believed that by obtaining this information the nurse will become a better assistant to the surgeon and not one who merely follows instructions. The nurse is expected to be on the lookout for unusual signs and symptoms, to observe the effect of drugs and procedures, and to use her own initiative in the event of a crisis.

There are chapters on inflammation, wounds, burns, ulcers and gangrene, tumors, anesthesia, and pre-operative and postoperative care of surgical patients.

Surgery of the various regions of the body is discussed as are fractures, diseases of the bones and joints, deformities, and the application of physical therapy to surgery. A brief description of the principles of nursing that may be of particular interest in handling each type of surgery, is given, but the actual technique of nursing and nursing procedure are not included in the book.

This work is an effort to satisfy the authors' belief that nurses in the better schools are as well grounded in the sciences fundamental to medicine as were the medical students of 10 years ago and that the nurses are eager for accurate knowledge pertaining to the field of surgery.

The inclusion of diagnostic methods with the technique of operative and manipulative treatment of surgical conditions, the dosage of drugs in many instances and the descriptions of such operations, with drawings, as division of the sensory root of the trifacial nerve, operation for aneurism, radical removal of the breast, and certain minor procedures done by a general practitioner might lead one to question the choice of teaching material for other than medical students.

G. L. MCWHORTER.

THE second edition of Zondek's valuable and extensive monograph[3] is introduced by a short essay on fallacious methods of hormone research that might well be applied to general scientific medical investigations,—"Verlasst man sich also nur auf die klinische—an Fehlerquellen reiche—Beobachtung, so kann der unkritische spielend Theorien machen und seiner Phantasie weiten Spielraum geben." The material presented is, thus, mainly a record of physiological research. An exhaustive review is given of the assay, source, preparation, biological action, occurrence in the male, fate, and hormone interrelations of estrogenic substances. The pituitary gonadotropic hormones are then taken up in the same way. The interplay of the pituitary and gonad is then thoroughly studied. Clinical determination of folliculin and prolan in the blood and urine is described. Polyhormonal menstrual disorders are discussed. The occurrence of pituitary follicle stimulating hormone is given and its excretion in male and female genital malignancy described. The clinical use of estrogenic and pituitary substances is covered. Reviews of the hormone diagnosis of pregnancy and Zondek's studies of inter-

[1] GYNECOLOGICAL AND OBSTETRICAL TUBERCULOSIS. By Edwin M. Jameson, B.S., M.D. Philadelphia: Lea & Febiger, 1935.

[2] THE PRINCIPLES AND PRACTICE OF SURGICAL NURSING. By Charles D. Lockwood, A.B., M.D., F.A.C.S., and John A. Wolfer, M.D., F.A.C.S. In collaboration with Mildred E. Newton, B.S., R.N. 2d rev. ed. New York: The Macmillan Co., 1935.

[3] HORMONE DES OVARIUMS UND DES HYPOPHYSENVORDERLAPPENS; UNTERSUCHUNGEN ZUR BIOLOGIE UND KLINIK DER WEIBLICHEN GENITAL FUNKTION. By Dr. Bernhard Zondek. 2d enl. ed. Wien: Julius Springer, 1935.

medin, the hormone of the middle pituitary, conclude the work. PAUL STARR.

FRACTURES and dislocations are discussed in detail in Kellogg Speed's[1] *Text-Book of Fractures and Dislocations*, not only to their mechanism but also as to diagnosis and treatment. Illustrations are shown of modern apparatus and their application. Each type of fracture is thoroughly covered as to method of reduction, kind of anesthesia (local or general), and as to open and closed methods of reduction.

It is my opinion that this is the most complete book on fracture that has been written; it is really a postgraduate course in modern diagnosis and treatment of fractures. The book is an encyclopedia on fractures; careful reading to digest each word will enable one to gain full knowledge of the subject.

JAMES J. CALLAHAN.

[1] A TEXT-BOOK OF FRACTURES AND DISLOCATIONS; COVERING THEIR PATHOLOGY, DIAGNOSIS, AND TREATMENT. By Kellogg Speed, S.M., M.D., F.A.C.S. 3d ed. thoroughly rev. Philadelphia: Lea & Febiger, 1935.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

OXFORD MEDICAL PUBLICATIONS. The Early Diagnosis of the Acute Abdomen. By Zachary Cope, B.A., M.D., M.S. Lond., F.R.C.S. Eng. 7th ed. New York: Oxford University Press, 1935.

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SOCIAL SECURITY. By Edward H. Ochsner, B.S., M.D., F.A.C.S. Chicago: The Social Security Press, 1936.

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DIAGNOSTIC ROENTGENOLOGY. Ross Golden, M.D., Editor. New York and Edinburgh: Thomas Nelson & Sons, 1936.

OXFORD MEDICAL PUBLICATIONS. Painful and Dangerous Diseases of the Ear; a Text-book for Students and General Practitioners. By R. R. Woods, M.B., F.R.C.S.I. London: Oxford University Press, 1936.

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PATOLOGIA QUIRURGICA. Craneo-Cara-Raquis-Cuello. By Dr. Conrado Zuckermann.

LE TRAITEMENT CHIRURGICAL DU GOITRE EXOPHTHALMIQUE ET DES GOITRES AVEC HYPERTHYROIDIE. By Louis Courty and M. Ansel. Paris: G. Doin et Cie, 1936.

ABORTION; SPONTANEOUS AND INDUCED; MEDICAL AND SOCIAL ASPECTS. By Frederick J. Taussig, M.D., F.A.C.S. Sponsored by The National Committee on Maternal Health, Inc. St. Louis: The C. V. Mosby Co., 1936.